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IS THERE MORE THAN ONE KIND OF RICKETS?*

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For at least two years our attention has been attracted to the possibility of the existence of more than one kind of rickets. That is, under the head of rickets may be included more than one kind of disturbance of the mineral metabolism of the body which manifests itself in a characteristically defective growth and calcification of the bones. The possibility was suggested by a series of clinical observations concerning the association of rickets with other diseases or pathological conditions and certain peculiar manifestations of rickets itself in some children. Inasmuch, however, as the idea of the duality or multiplicity of rickets rested solely on clinical observations which, at most, were only of a suggestive nature, we have never felt justified in presenting it as a definite hypothesis. But, recently, our experiments with the rat have yielded results which strongly suggest that there may be two distinct forms of the disease.

EXPERIMENTAL EVIDENCE

In previous publications [1] we have described certain defective diets which, when fed to the young rat, produce marked disturbances in

* Received for publication Jan. 4, 1922.

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1. Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, Nina: Studies on Experimental Rickets. III. A Pathological Condition Bearing Fundamental Resemblances to Rickets of the Human Being Resulting from Diets Low in Phosphorus and Fat-Soluble A: The Phosphate ion in Its Prevention, Johns Hopkins Hosp. Bull. **32**:160 (May) 1921. McCollum, E. V.; Simmonds, Nina; Shipley, P. G., and Park, E. A.: VI. The Effects on Growing Rats of Diets Deficient in Calcium, Am. J. Hygiene **1**:492 (July) 1921. McCollum, E. V.; Simmonds, Nina; Shipley, P. G., and Park, E. A.: VIII. The Production of Rickets by Diets Low in Phosphorus and Fat-Soluble A, J. Biol. Chem. **47**:507 (Aug.) 1921. Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, Nina: XVII. Am. J. Hygiene **2**: 1922.

the growth and calcification of the skeleton. The diets in question were alike in being insufficiently supplied with a factor or factors present in cod liver oil but differed from each other considerably in the composition of their mineral fraction, chiefly as regards the calcium and phosphorus. They may be divided into two groups according to the relative amounts of those two elements present. In one group the phosphorus was at a low level but the calcium at or above the level which would be optimal if all other dietary factors were satisfactory. In the other group the calcium was at an extremely low level but the phosphorus was not far from the optimal.

When the diets of the first group (those in which the phosphorus was deficient and the calcium phosphate ratio high) were fed to young rats living under ordinary laboratory conditions (room light), a pathologic condition of the skeleton developed, identical in all essential particulars with that seen in the rickets of human beings. The costochondral junctions were greatly enlarged; in some animals the thoracic wall was sunken at the sites of the costochondral junctions; the shafts of the ribs were fractured (Fig. 1). The long bones of the extremities were enlarged at the ends and could be cut easily. Between shaft and cartilage was a yellowish-white zone from two to three millimeters deep—the rachitic metaphysis. The proliferative cartilage extended in irregular prolongations toward the shaft. Calcium deposition in the cartilage was entirely lacking or extremely defective. The intermediate zone between cartilage and shaft was of a composition identical with that found in the metaphysis of the bones of rachitic children. It was composed of: cartilage in all stages of metaplasia or degeneration into a material indistinguishable from the osteoid; trabeculae consisting of osteoid; blood vessels; marrow elements; scattered, irregular deposits of calcified material encased in osteoid; and connective tissue. These were intermingled in a disorderly manner. The trabeculae of the shaft were surrounded by broad investments of osteoid (Figs. 2, 3 and 11).

When the diets of the second group (those in which the calcium was deficient, the phosphorus at a level not far from the optimal and the calcium-phosphate ratio low) were fed to rats kept under ordinary laboratory conditions (room light), a diseased condition of the skeleton developed which also bore marked resemblances to the lesions found in the rickets of human beings. The gross deformities caused by the second group of diets were as great or greater than those caused by the first group and corresponded exactly to the deformities found in rachitic children. The thorax was even more deformed than in the rats fed the diets of the first group; it was flattened from side to side and marked by deep grooves which followed the costochondral junc-

tions; the angular deformities produced at the junction of the costal cartilages and the shafts projected into its interior; the costochondral junctions were enlarged and greatly distorted; fractures in the shafts of the ribs were especially numerous (Fig. 4). The lower ends of radius and ulna were enlarged as were also the ends of all the long bones of the extremities and the bones were extremely soft and weak. Between the cartilage and the shaft was a white intermediate zone one to three millimeters deep. Microscopic examination showed that the cartilage was entirely or nearly free from calcium and was invaded in

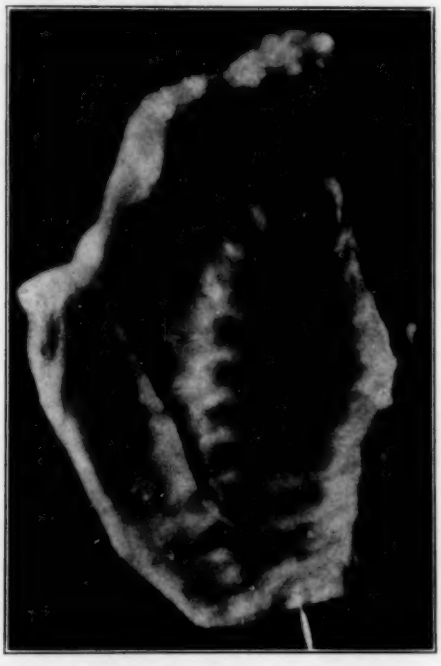

Fig.1.—Pleural aspect of thorax of a rat which had developed rickets on diet 3,143 high in calcium and proportionately low in phosphorus.

an irregular manner by the vascular elements of the shaft. In consequence, the cartilage extended toward the shaft in irregular prolongations. The cells of the cartilage in proximity to the shaft showed evidences of degeneration and metaplasia. The intermediate zone was composed of cartilage in a more or less degenerated state, osteoid trabeculae, blood vessels surrounded by marrow elements, and a few deposits of calcium for the most part situated near the periphery and connective tissue. The trabeculae of the shaft were bordered by rather broad zones of osteoid. A loosely arranged fibrous tissue invested many of the trabeculae and in those places in which it filled in the

spaces between the trabeculae, it gave rise to histologic pictures which closely resembled those furnished by the fibrous marrow in the rickets of human beings (Figs. 5, 7, 8 and 10).

The pathologic condition induced in the bones by the diets of the second group did not, however, correspond at all points to that usually found in the human subjects of the disease. The metaphysis was composed in larger part of osteoid trabeculae. Though these osteoid trabeculae

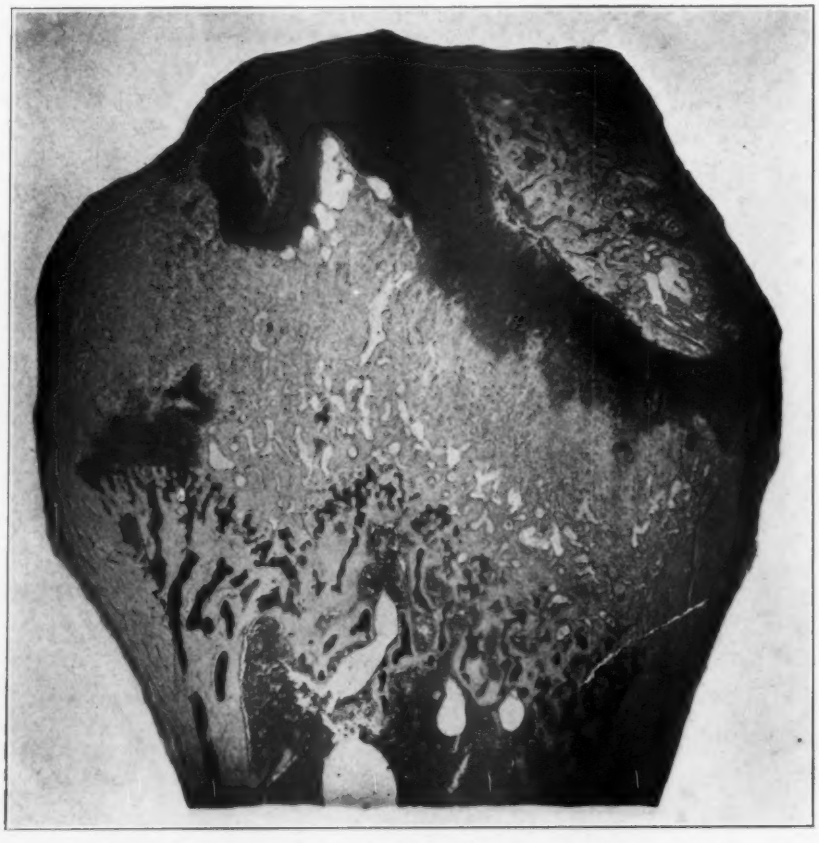

Fig. 2.—Microphotograph of a bone showing low phosphorus rickets. Note the lack of calcification of the cartilage, the very wide metaphysis, and the osteoid tissue surrounding the calcified trabeculae of the shaft.

were free from calcium deposition, they nevertheless retained a certain semblance of orderly arrangement. The osteoid zones about the trabeculae were not always so broad as in the rats on the diets of the first group, though they were quite as broad as the osteoid borders in the bones of rachitic children (Figs. 6 and 7). Cells evidently

derived from the fixed tissues with large basophilic granulations were numerous in the immediate vicinity of the trabeculae (Fig. 9). Resorptive activity was exceedingly marked.

The abnormal condition of the skeleton produced by the faulty diets of the second group corresponded to that found in human beings with rickets in all fundamental respects, namely, the degenerative and metaplastic changes of the cartilage, the complete absence or defective character of the calcification of the cartilage, an abnormal amount of

Fig. 3.—High calcium rickets in an animal on diet 3,133. This diet contains 2 per cent. added calcium carbonate instead of 3 per cent., as in diet 3,143. Note the linear deposit of calcium in the metaphysis, which marks an abortive attempt to heal.

osteoid production, irregular invasion of the cartilage, and the production of a rachitic intermediary zone. While one of the diets in question (diet 2638) did not give absolutely constant results in all animals, in some it produced a pathologic condition corresponding to that found in rickets of human beings even in its minor details.

DISCUSSION

Our experiments make it clear that, when the rat is deprived of certain active light rays and an unidentified factor contained in cod liver oil, a pathological condition corresponding in all fundamental respects to rickets in human beings can be produced through the diet in two ways: (1) by diminishing the phosphorus and supplying an optimal amount or an excess of calcium, or (2) by reducing the calcium and maintaining the phosphorus at a concentration somewhere near the optimum. In the first the calcium: phosphate ratio is large, in the second small. We are certain that in the human being similarly deprived of light and the unidentified factor it would also be possible to produce true rickets through a manipulation of the calcium and phosphate of the diet in the two ways mentioned.

Fig. 4.—Pleural aspect of thorax of a rat which had developed low calcium rickets on diet 2,638, which is high in phosphorus relatively, and low in calcium.

As a result of our experiments we are led to believe that there are two main kinds of rickets. One is characterized by a normal or nearly normal blood calcium and a low blood phosphorus (low phosphorus rickets); the other by a normal or nearly normal blood phosphorus but a low blood calcium (low calcium rickets). The investigations of Howland and Kramer [2] and of Kramer, Tisdall and Howland [3] on

2. Howland, J. and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

3. Kramer, B.; Tisdall, F. F., and Howland, J.: Observations on Infantile Tetany, Am. J. Dis. Child. **22**:431 (Nov.) 1921.

the calcium and phosphorus content of the blood serum in rickets and tetany have given suggestive evidence in support of this idea. These observers found that in children suffering from rickets alone, the phosphorus of the blood serum is low, and the calcium not far removed from the normal; in children suffering from manifest tetany complicating rickets, on the other hand, the calcium is low but the phosphorus not far removed from normal.

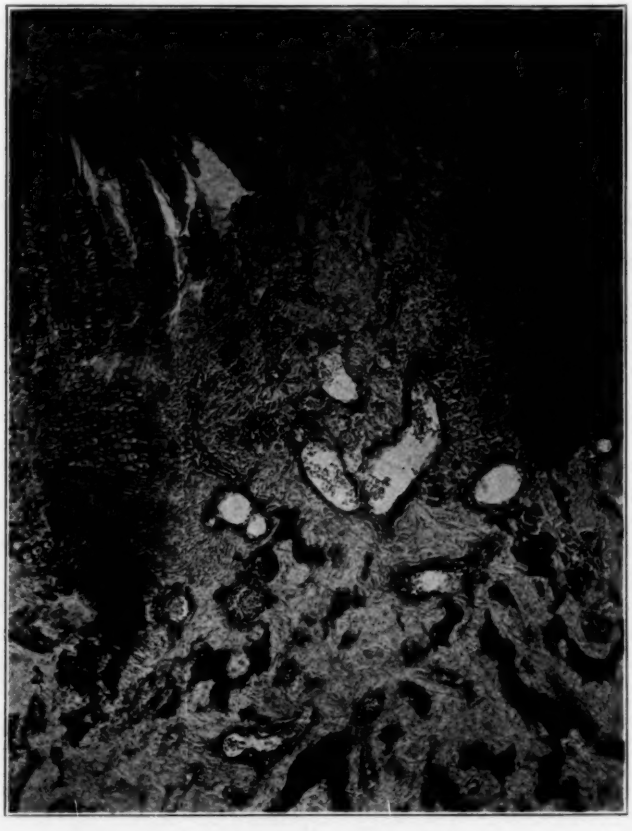

Fig. 5.—Low power microphotograph showing low calcium rickets. The cartilage is extremely irregular, and many cells have undergone metaplasia into osteoid tissue. There are long tongues and islands of cartilage to be seen in the metaphysis, which contains almost no calcified bone. Magnification × 70.

Rickets and Tetany.—As is well known, tetany complicates certain cases of rickets but not by any means all. Cases of rickets, even very severe rickets, exist in which tetany does not supervene, and, in all likelihood, never will. In other cases of rickets tetany either in the

manifest or in the latent form is present for weeks and numerous observers have pointed out that it is with the less severe forms of rickets that tetany usually allies itself. Furthermore, experience has shown that a cure in rickets accompanied by tetany is most easily accomplished through the administration of calcium and cod liver oil or calcium and heliotherapy, whereas in rickets uncomplicated with tetany the cure is most readily accomplished by means of the administration of cod liver oil or heliotherapy with or without phosphate. The

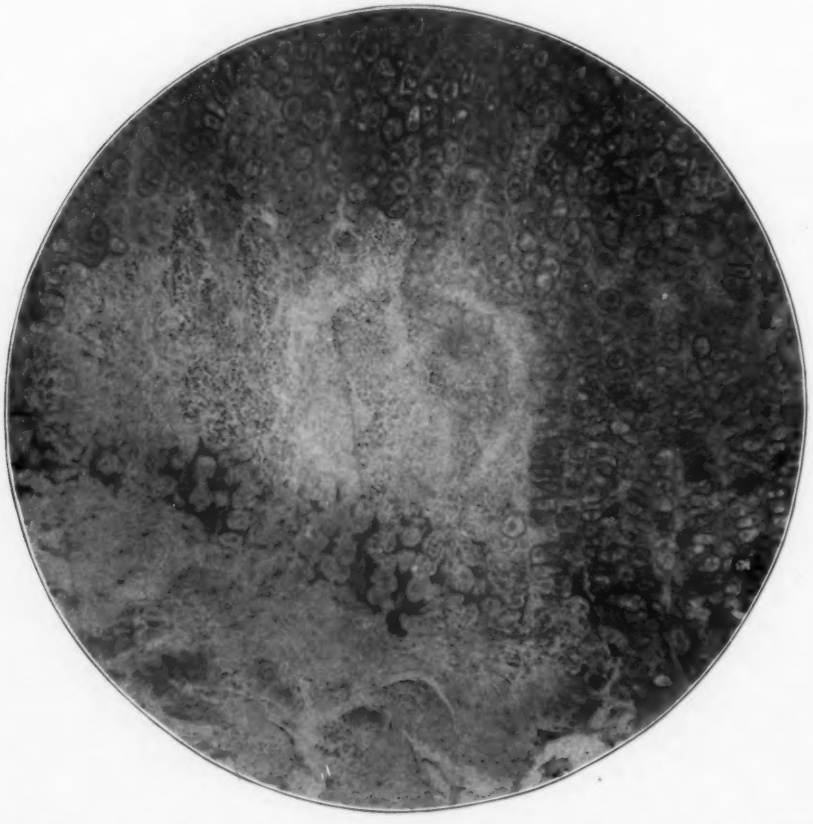

Fig. 6.—Microphotograph showing detail in the metaphysis of the bone (Fig. 3). Note the invasion of the cartilage by blood-vessels, its prolongation into the metaphysis, and the line of calcification (Ca) in the metaphysis which marks the occurrence of an aborted healing process.

chemistry of tetany, its occurrence in some cases of rickets but not in all, and the fact that the successful form of treatment differs with the presence or absence of tetany, rather strongly suggest that rickets with tetany and rickets without tetany are distinct forms of metabolic disturbance affecting the skeleton.

Recently Huldschinsky [4] has advanced the view that tetany is nothing more or less than a symptom complex of healing rickets. While it is possible for tetany to occur with a healing rickets, clinical observation alone is enough to show that tetany does not ordinarily have that relationship to the disease. We have repeatedly seen children with rickets of the greatest severity undergo treatment with cod liver oil and have followed the healing process in the bones by means of the roentgen ray. None of the children ever showed the slightest evidence of tetany during the process of cure.

Fig. 7.—Low calcium rickets in the bone of an animal on diet 2,638.

It is undoubtedly true, however, that in some cases of rickets accompanied by tetany the roentgen ray shows deposition of lime salts at the cartilage-shaft junctions of the long bones of the extremities. The reason for this, according to the present trend of our investigations, is in many instances as follows: In the low calcium and the low phosphorus forms of rickets, calcium: phosphate ratios exist in

4. Huldschinsky, K.: Die Beeinflussung der Tetanie durch Ultravioletlicht, Ztschr. f. Kinderh. **26**:5, 1920.

the blood which do not permit at all or permit only to a very limited extent the deposition of calcium phosphate in the bones. Between the low calcium form of the disease and the normal condition, on the one hand, and the low phosphorus form and the normal condition on the other, are innumerable gradations, presumably characterized by calcium: phosphate ratios in the blood, very probably oscillating ratios, which permit calcium phosphate deposition in varying degree, from the most

Fig. 8.—Low calcium rickets from a rat on diet 3,041. This diet contains the same amount of calcium as diet 2,638, but the phosphate content of the diet is slightly higher.

fragmentary to almost complete calcification (Figs. 3 and 6). In connection with both the low calcium and the low phosphorus forms of rickets, therefore, there are borderline states of the disease in which the calcium: phosphate ratios are such as to permit calcium phosphate deposition to take place irregularly or intermittently in the bones. With the borderline cases, in particular those connected with the low calcium form of the disease, we believe tetany to be frequently associated.

Our experiments indicate that deposits of calcium salts at the epiphyseal line may occur as a result of (1) healing in the low phosphorus form of rickets, (2) healing in the low calcium form and (3) as a constantly occurring or recurring phenomenon in the borderline states of the disease. With the first we believe that tetany is rarely associated and then, usually certainly, only in the latent form; with the second, tetany may be associated; with the third we believe it to be frequently associated.

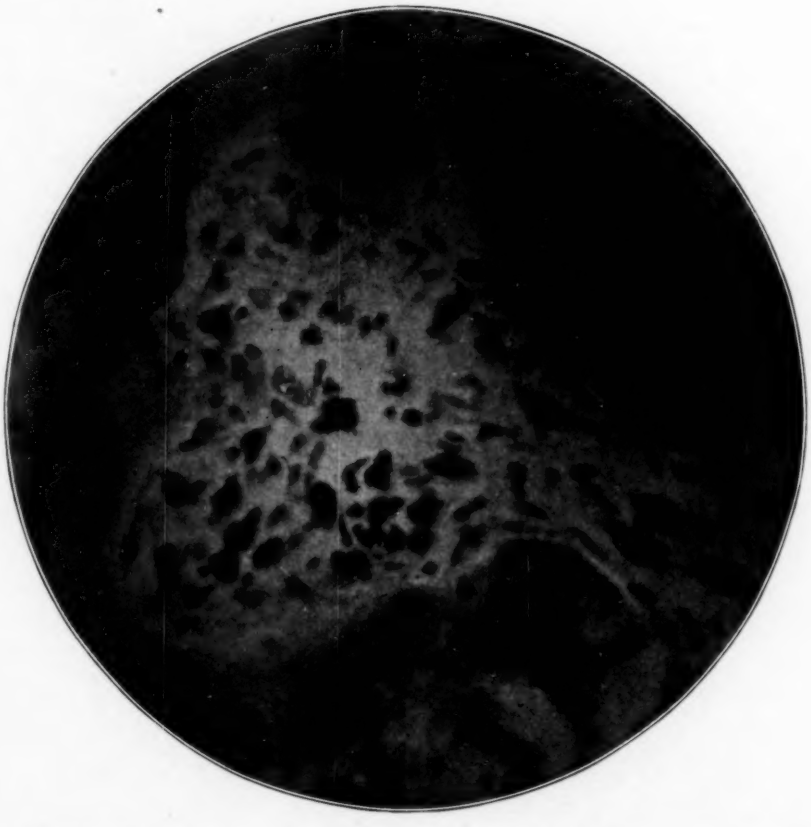

Fig. 9.—High power microphotograph showing basophil connective tissue cells near the trabeculae of bone in the shaft of an animal with low calcium rickets, diet 3,141.

According to present knowledge, the relationship between tetany and rickets appears to be as follows: Tetany is an expression on the part of the nervous tissues of an insufficiency of the calcium ion; rickets is an expression on the part of the skeleton of disturbed relations between the calcium and phosphate ions. The reason that tetany is so frequently associated with rickets is because rickets is a

disease in which the calcium ion in the body tissues and fluids is subject to wide variations. Tetany occurs independently of rickets, just as rickets occurs independently of tetany. Since tetany may occur with the low phosphorus form of rickets, it does not serve to mark off one form of rickets from the other. Tetany is essentially associated, however, with the low calcium form, and, for all practical purposes, the low calcium form of rickets is the rickets of tetany.

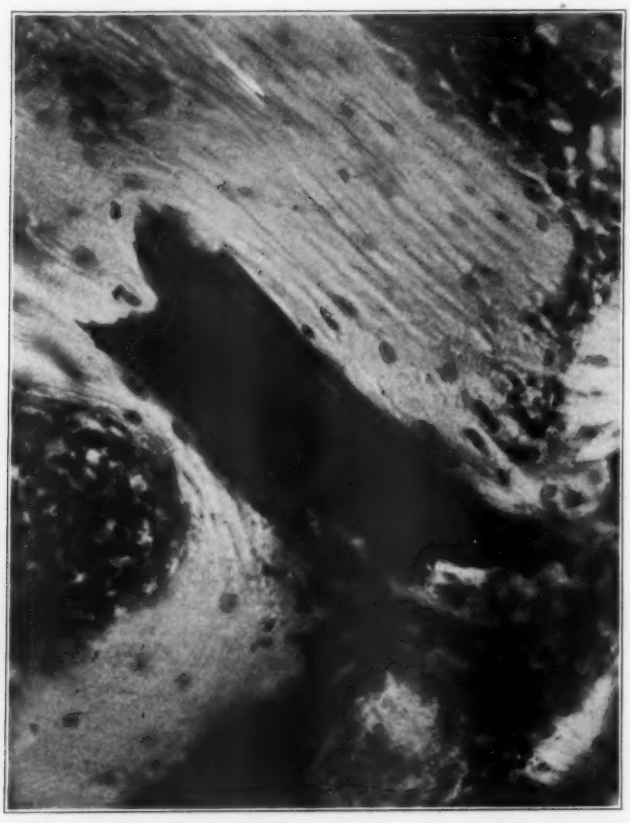

Fig. 10.—High power microphotograph to show the osteoid tissue from a case of low calcium rickets. Magnification × 375.

Rickets and "Renal Dwarfism."—Recently Barber, Patterson and others have described children and young adults who were undersized, had rachitic deformities, and at the same time were the subjects of severe forms of chronic interstitial nephritis or developmental defects of the kidney. To the syndrome of symptoms which they exhibited, Barber gave the name "renal dwarfism." The age of one of Patterson's patients was only one year and 9 months, but all others were

between 6 and 20 years of age. If the infant described by Patterson be excepted, the height was from 6 to 16 inches under the average for the age, and the rickets was peculiar in that it was a late and gradual development (rachitis tarda). The disturbance of renal function in some of the cases was known to be extreme.

We have seen a child, aged 3½ years, whose case belongs in this category. The rachitic deformities were extreme. Moreover, the changes in the bones, as revealed by the roentgen ray and histologic examination, were most extensive and differed from the changes ordinarily found in rickets. The proliferative cartilage was most

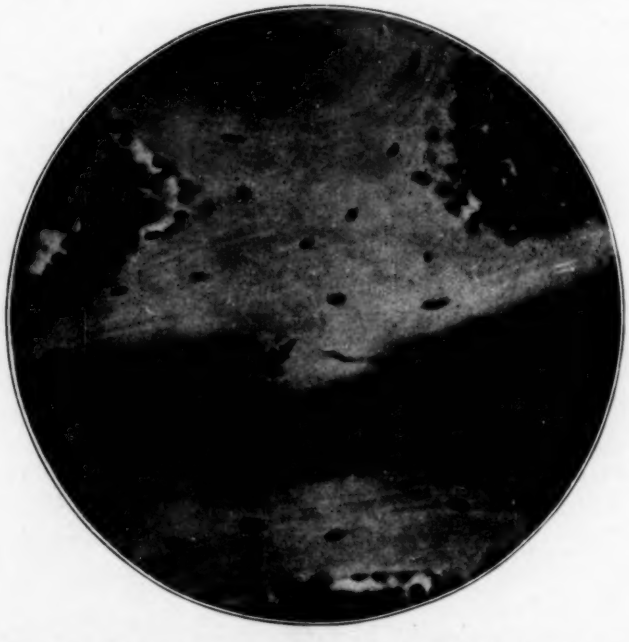

Fig. 11.—This picture shows an osteoid and calcified bone in a trabecula from a case of low phosphorus rickets. Animal was on our diet 3,143. Same magnification as in Figure 10.

irregular and the calcification defective. In the deep metaphysis were large islands of cartilage bordered on one or more sides by dense calcium deposits. Those islands of cartilage gave to the metaphysis, as seen in the roentgenogram, a honeycomb appearance. The trabeculae were thin and the osteoid borders, comparatively speaking, narrow. Surrounding the trabeculae and islands of cartilage and lying between them was a loose fibrous tissue. Obviously, for a long time the pathologic condition in the bones had been in a state of flux between healing and relapse. The specific gravity of the urine was low and

appeared to be fixed. Albumen was constantly present. Several attacks which were thought to be uremic acidosis occurred. After death the kidneys were found to be exceedingly small and were defectively developed.

The histologic condition found in the bones of the infant described by Patterson appears to have been exactly similar.

It seems possible to us that the rickets which develops in the subjects of "renal dwarfism" has its origin in the extreme functional disability of the kidney and may belong to the low calcium form of the disease, i. e., that it may be dependent on an inability of the kidney properly to excrete phosphate. If our suggestion should prove to be correct, a true "renal rickets" exists and rickets under certain conditions may have an endogenous origin.

The Rickets Occurring in Children Suffering from the Severer Secondary Anemias.—Some infants develop a marked anemia which is apparently independent of concurrent infection. In many instances, it seems probable that this anemia is of dietetic origin, since breast feeding, or a diet almost entirely composed of cow's milk, has been unduly prolonged. The blood picture is that of a secondary anemia but sometimes corresponds to the picture generally known as von Jaksch's anemia. The children showing this abnormal condition of the blood regularly show rickets. The rachitic deformities are, however, somewhat different from those ordinarily seen and are fairly uniform. The frontal and parietal eminences are large and the regions of the sagittal and coronal sutures often appear sunken. The enlargement of the costochondral junctions and the ends of the long bones of the extremities is moderate and the degree of involvement at the cartilage-shaft junctions does not seem to be advanced. The involvement of the skull appears to be out of proportion to the involvement of the bones of the extremities or of the thorax.

We can form no definite idea concerning the nature of the disturbance in the metabolism which causes the rickets in the children suffering from severe secondary anemia. Probably the rickets and the anemia have a common origin, or are connected in some way. In any event it is interesting that in a recent series of experiments Happ [5] was able to produce the most severe anemia and rickets in the rat by feeding certain diets extremely low in calcium. The experiments of Happ might indicate, therefore, that the rickets accompanying the severe so-called "alimentary" anemias belong to the low calcium form of the disease. Children showing the peculiar combination in question, however, failed to show evidences of tetany. It seems to us possible that the rickets accompanying the alimentary anemias may represent

5. Happ, W. M.: In press (Personal communication).

a somewhat different kind of disturbance in the mineral metabolism from the ordinary forms of the disease. Evidently another tissue, the blood, which is not regularly affected in rickets, is included in the metabolic disturbance.

We are prepared to find the etiology of rickets as varied as the etiology of tetany. Tetany was once considered to be an entity. Now, it is necessary to regard it as a symptom complex which can be produced experimentally in a variety of ways and which occurs naturally in several conditions. Tetany may be produced by excision of the parathyroid glands, by the injection into the blood stream of sodium phosphate or of sodium bicarbonate, by diets high in sodium phosphate and by the creation of gastric fistula which result in the loss of the gastric secretions. It occurs spontaneously in association with rickets and sometimes dilatation of the stomach. We should suppose that any influence which would result in the depression of the calcium or the phosphorus ions in the body fluids with the formation of the calcium: phosphate ratios favorable for the development of rickets if continued long enough would produce the disease and that there might be several such influences.

CONCLUSIONS

1. Our experiments make it clear that when the rat is deprived of certain active light rays and an unidentified factor contained in cod liver oil, a pathologic condition corresponding in all fundamental respects to rickets in human beings can be produced through the diet in two ways: (1) by diminishing the phosphorus and supplying the calcium in optimal quantities or in excess, or (2) by reducing the calcium and maintaining the phosphorus at a concentration somewhere near the optimum.

2. We believe it to be certain that in the human being, similarly deprived of light and the unidentified factor, it would also be possible to produce true rickets through an adjustment of the calcium and phosphorus of the diet in the two ways mentioned.

3. As the result of our experiments we are led to believe that there are two main kinds of rickets. One is characterized by a normal or nearly normal blood calcium and a low blood phosphorus (low phosphorus rickets); the other by a normal or nearly normal blood phosphorus but a low blood calcium (low calcium rickets).

4. If the hypothesis just stated is correct, the relation of tetany to rickets would appear to be as follows: Tetany is essentially an expression on the part of the nervous tissues of an insufficiency of the calcium ion; rickets is essentially an expression on the part of the skeleton of disturbed relations between the calcium and phosphate ions of the body fluids. Tetany is frequently associated with rickets

because rickets is a disease in which the calcium ion in the body tissues and fluids is subject to variations. Tetany occurs independently of rickets, just as rickets occurs independently of tetany. Since tetany may occur with the low phosphorus form of rickets, it does not serve to mark off one form of rickets from the other. Tetany, however, is essentially associated with the low calcium form of rickets, and, for all practical purposes, the low calcium form of rickets is the rickets of tetany.

5. It seems possible that the etiology of rickets may be as varied as the etiology of tetany. Our experiments lead us to suppose that in the absence of certain active light rays and an unidentified dietary factor contained in cod liver oil, any influence which would result in the depression of the calcium or phosphate ions in the body fluids with the formation of calcium : phosphate ratios favorable for the development of rickets would ultimately produce the disease. We are prepared to think that there may be several such influences.

6. For some time, as the result of clinical observations concerning curious associations of rickets with other pathologic conditions and certain peculiar manifestations of the disease in some children, our attention has been attracted to the possibility of the existence of more than one kind of rickets. In the light of our experiments we suggest the possibility that there may be a true renal rickets and that the rickets accompanying the alimentary anemias may represent a somewhat different kind of disturbance in metabolism from that which is present in the ordinary forms of the disease.

THE VALUE OF THE ROUTINE USE OF THE COLLOIDAL GOLD REACTION IN ACUTE EPIDEMIC POLIOMYELITIS*

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In 1916 Johnston [1] reported on the use of the colloidal gold test on the spinal fluid in four cases of poliomyelitis. He found an early transitory reaction in the syphilitic zone during the acute stage, and he considered that the test might prove an important aid in diagnosis. In March, 1917, Felton and Maxcy [2] published an excellent and important contribution on the subject. These investigators examined the spinal fluids of fifty-seven patients during various stages of the disease, and came to the following conclusions: (1) In the acute stage of poliomyelitis, the spinal fluid reacts with colloidal gold in dilutions of 1:40 to 1:60 producing a maximum decoloration of 3. (2) In the second and third weeks the reaction is practically the same, with a tendency to clear up in some cases and a precipitation in higher dilutions in others. (3) From the fourth to the eighth week, the curve runs practically parallel to the globulin and albumin content, persisting to the eighth week and beyond but still occurring in dilutions of from 1:40 to 1:60. (4) As the reaction is constantly in the same zone, the test is helpful in diagnosis.

Jeans and Johnston [3] in the same month (March, 1917), reported the results of the examination of the cerebrospinal fluid in 100 cases of poliomyelitis in the acute stage. Fifty-five patients had definite paralysis and the fluids of the entire fifty-five gave a definite reduction of the gold chlorid solution in low dilutions of the spinal fluid. This reaction occurred with such uniformity that they believe the test is of distinct value in the diagnosis of poliomyelitis. In a few abortive cases and those in the preparalytic stage, the curve was not essentially different from that obtained in the clear cut paralysis cases. Jeans and Johnston emphasize the value of the test as a means of differential diagnosis from meningismus and other forms of meningitis.

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1. Johnston, M. R.: Am. J. Dis. Child. **12**:112 (Aug.) 1916.
2. Felton, L. D., and Maxcy, K. F.: J. A. M. A. **68**:752 (March 10) 1917.
3. Jeans, P. C., and Johnston, M. R.: Am. J. Dis. Child. **13**:239 (March) 1917.

Neal and Abramson[4] in a detailed and careful study carried out during the 1916 epidemic on the spinal fluid in poliomyelitis, reported, among other tests, the results obtained with the colloidal gold reaction. They examined 114 cases, and found the result in seventy-seven of the fluids to fall in one of six curves as follows:

In 40 cases	1122100000	In 5 cases	1121100000
In 8 cases	1123210000	In 14 cases	1111000000
In 6 cases	1112210000	In 4 cases	1121000000

The remaining thirty-seven fluids gave various curves similar to the six foregoing but not exactly classifiable under any of the headings. The composite curve of the 114 spinal fluids was 1122100000. Neal and Abramson did not consider the gold chlorid reaction of absolute diagnostic value since they found that a few of the fluids from epidemic or tuberculous meningitis cases may also fall in these groups. They emphasize the fact that in only one instance was a poliomyelitis fluid negative, even in the case of fluids with normal chemistry, while the curves from cases of meningismus have been normal, even with a slightly increased chemistry, although not a sufficient number of fluids had been examined to be sure that this latter fact holds true in all cases.

Kolmer, Freese, Matsunami and Meuse,[5] in a somewhat similar study of the spinal fluid from poliomyelitis cases, examined the fluids from thirty-eight cases by this reaction. The fluids from eighteen cases, removed from the second to the twelfth day after the onset of the paralysis, showed no color change at all; in four cases in the same stage there was only a slight precipitation in the first two tubes 1100000000—while all these fluids showed an increase in cells, and one of them in globulin. The fluids from ten cases, examined from two to twelve days after onset, yielded reactions of the syphilitic zone type with maximum precipitation in from 1:40 to 1:160, and decolorization usually terminating with blue. The fluids from six cases examined from twelve to nineteen days after the onset of paralysis yielded reactions of the meningitic zone type, characterized by maximum precipitation in from 1:80 to 1:320 to 1:640. In conclusion, Kolmer and his collaborators state that during the acute stage of poliomyelitis the fluid from 40 to 50 per cent. of the cases yielded a colloidal gold curve in the syphilitic and meningitic zone; a peculiar or definite curve of precipitation was not obtained by them.

Overholser[6] applied the colloidal gold test to twenty-one specimens of spinal fluid from cases of poliomyelitis. Fourteen, or 66

4. Neal, J. B., and Abramson, H. L.: Arch. Int. Med. **19**:341 (Sept.) 1917.
5. Kolmer, J. A.; Freese, A. E.; Matsunami, T., and Meuse, B.: Am. J. M. Sc. **154**:720, 1917.
6. Overholser, W.: Boston M. & S. J. **177**:480 (Oct. 4) 1917.

per cent., gave a typical curve of the acute stage (112331000), the other curves were so anomalous that this investigator believed some technical error must be invoked to explain them. Larkin and Cornwall [7] examined fifty spinal fluids by the colloidal gold test. In only two was a normal reaction obtained; 63 per cent. of the curves were humped, but they did not note any curve which was diagnostic of poliomyelitis. They found no parallelism to exist between the colloidal gold curve and the other spinal fluid or blood findings, but believed there was probably a tendency for the height of the curve to increase with the severity of the infection. Carr,[8] in writing of the same series of cases, states that the reaction was in the syphilitic zone in 70 per cent. of the cases and that low curves were the rule. Vogel,[9] in a general report of his work with this test, gives the result of its application in three cases of poliomyelitis; in one the curve was in the paretic zone and in two it was of a syphilitic type.

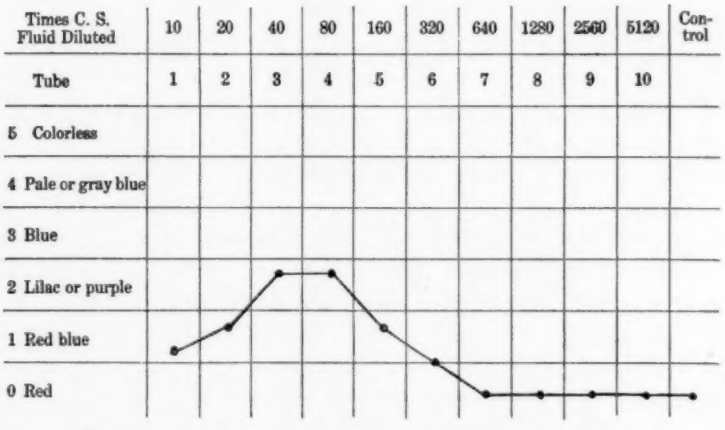

Fig. 1.—Average curve in first week of the disease.

During 1920, a small localized outbreak of poliomyelitis occurred in Brooklyn, and the Kingston Avenue Hospital admitted nineteen cases from August 24 to November 26. Subsequently two additional cases were received, making a total of twenty-one. In this series there were four fatalities, due to poliomyelitis, the four patients entering the hospital on or about the same date (November 11). The predominant type of the disease was that usually seen, the spinal or myelitic, with, however, an unusually high percentage of cases with moderate or marked polyneuritic symptoms, which in a few instances made up the most pronounced features of the malady.

7. Larkin, J. H., and Cornwall, L. H.: Arch. Pediat. **35**:459, 1918.
8. Carr, W. L.: Arch. Pediat. **34**:591 (Aug.) 1917.
9. Vogel, K. M.: Arch. Int. Med. **21**:496 (Oct.) 1918.

The colloidal gold reaction was performed in each of the twenty-one cases included in our series, and a total of seventy-four spinal fluids from these twenty-one patients were examined in various stages of the disease from the fourth to the one hundred and twenty-third day. Classified according to the week in which they were taken, the fluids were divided as follows:

First week	6 fluids	Eighth week	5 fluids
Second week	11 fluids	Ninth week	5 fluids
Third week	11 fluids	Tenth week	4 fluids
Fourth week	7 fluids	Eleventh week	3 fluids
Fifth week	6 fluids	Fourteenth week	1 fluid
Sixth week	10 fluids	Eighteenth week	1 fluid
Seventh week	4 fluids	Total	74 fluids

Results Obtained.—In this series, in no instance was the colloidal gold reaction normal when the spinal fluid was examined during the first three weeks of the disease. The curve obtained was constantly in the same zone.

In order to show the characteristics of the curve in poliomyelitis, we have separated our results according to the weeks of the disease in which they were obtained, and have on this basis separately constructed an average curve for each week up to the eighth. The curves for the first, second, fourth, sixth and eighth weeks are shown in Figures 1, 2, 3 and 4. These figures show the average characteristics of the reaction obtained at various periods of the disease in this series. It is noticeable that the curve for the first two weeks is very much the same, and is what we believe may be considered characteristic of this stage. In the first week it consists of an ascending curve presenting a gradual increase in reduction in higher dilutions starting in the reddish blue color in 1 : 10, extending into the lilac or purple color in 1 : 40 and 1 : 80, and then descending also gradually but more abruptly into the reddish blue again in 1 : 160 and reaching the nonreducing or red area in 1 : 640. In the second week, it differs only in that it remains in the lilac or purple area from 1 : 40 to 1 : 160.

As the disease progresses the average curve gradually falls, reaching normal in a minor proportion of the cases from the eighth to the ninth week of the malady. Thus, out of a total of ten fluids taken up to or beyond the ninth week, three showed a normal reaction before this period. One of these appeared on the twenty-eighth day, another on the fifty-third day, and a third on the fifty-fifth day. Of the seven fluids which remained elevated beyond the ninth week, three continued showing an acute poliomyelitis curve until the eleventh week, and one until the fourteenth week, to be exact, the one hundred and twenty-third day. In this series, therefore, 30 per cent. of the cases of poliomyelitis presented a normal reduction of colloidal gold at the end of the

ninth week. How long the curve remained elevated in the remaining 70 per cent. of the cases we were unable to determine, owing to the discharge of the patients from the hospital. We are cognizant of one case which is suggestive of the possible duration of a positive reaction in exceptionally severe attacks:

A young girl, 15 years of age, was admitted to the Kingston Avenue Hospital during the epidemic of 1916, with a very extensive paralysis involving the muscles of all the extremities, back and neck. After her discharge from the hospital, the patient had what she terms three relapses; in the first she was confined to bed two months, in the second for two years, and in the third for one year. She was admitted to the Kings County Hospital in 1920, suffering from chorea and residual paralysis of her left leg, back and some of the muscles of her neck. Two spinal fluids taken after admission showed a negative Wassermann, slight increase in cells and globulin, and a colloidal gold curve of 1122100000.

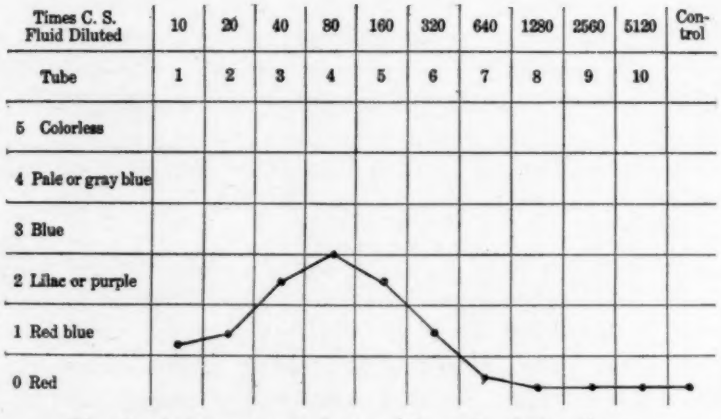

Fig. 2.—Average curve in second week of the disease.

This case is cited as an example of the possibility of a long persistence of colloidal gold reaction in a patient with severe infection. Of course, it cannot be absolutely proven that the curve was due to poliomyelitis, but the case is suggestive.

A very early subsidence of the curve, such as the twenty-eighth day (Case 1987) is exceptional. It occurred in a patient with moderate paralysis and slight polyneuritic involvement, who made a rapid recovery. On the other hand, patients with a persistence of a positive reaction of an acute type beyond the ninth week have usually presented a marked and extensive paralysis (Cases 1840, 1895 and 1990) with moderate or marked and persistent polyneuritis, or a mild paralysis with persistent and marked polyneuritis (Case 1011). It seems to us from this somewhat limited study, that there is a definite relationship between the duration of the positive colloidal gold reaction

and the persistence of polyneuritic symptoms and to a lesser extent paralysis. Patients who run an acute curve late in the disease usually present also some degree of persistence of the acute hydrocephalus which occur during the early weeks of the malady, and the fluid obtained on lumbar puncture continues to be increased in amount and in pressure. We are strongly inclined to believe that the period when the colloidal gold reaction returns to the normal indicates, as a rule, the end of the acute stage of the disease, and is, therefore, of great value in that one may determine more concisely than is done at present when the prolonged rest of the acute stage may be terminated, and the more active measures of treatment of the residual paralysis may be undertaken by massage, electricity, etc. The reaction seems to indicate better than any other means, such as the study of cytology and chemistry of the spinal fluid, or of the symptoms, when the acute generalized inflammation of the meninges, cord and brain has approximately subsided. It seems probable that all active methods of treatment for the subsequent paralysis are strongly contraindicated until this stage is passed. There is also another aspect, and that is that the extent of the paralysis which may remain and require treatment can best be judged when the reaction becomes normal, for throughout the period of its elevation great spontaneous improvement usually continues to occur.

In three of the seven cases presenting a curve beyond the ninth week, the reaction had begun to descend in the third or fourth week, but was subsequently found more elevated in the ninth, tenth or eleventh weeks. The average curve obtained, however, gradually falls as the disease advances. In the first and second weeks (Figs. 1 and 2) there is little variation. In the third week the average curve reaches high into the lilac area in 1:80 and the ascending line is definitely beginning to decline. In the fourth week (Fig. 3) there is a marked change in the curve consisting of a pronounced flattening out, and it is limited to the red blue area, from 1:10 to 1:320. From the fifth week to the ninth week (Fig. 4), the curve gradually continues to subside, the slight reduction obtained in the red blue color being gradually more and more limited to the lower dilutions.

There was only an inconstant relationship between the cytologic and chemical findings of the spinal fluid and the colloidal gold curve in this series. As a rule, as the reaction subsided, the globulin diminished, but, on the other hand, many cases presented a high curve late in the disease with a normal or almost normal globulin reduction. We did not note that in the first few weeks of the disease the augmentation of globulin and cells bore any relation to the height of the gold chlorid curve.

The average curve (Fig. 5) in the fatal cases is very similar to that obtained in the first and second weeks of the disease in the more severe nonfatal cases. Although in fatal cases it may tend to exhibit slightly greater precipitation and to be on the average a higher curve, there has not been sufficient difference in our series to make the test of any definite value from the prognostic viewpoint.

It is conceded by most workers who have studied the spinal fluid in cases of epidemic poliomyelitis, that there is nothing about the findings which is entirely characteristic of that disease. Thus, an increase in cells, lymphocytes or of globulin and a good (3+) reduction of Fehling's solution is merely confirmatory in a case in which the clinical diagnosis is clearly established. On the other hand, many

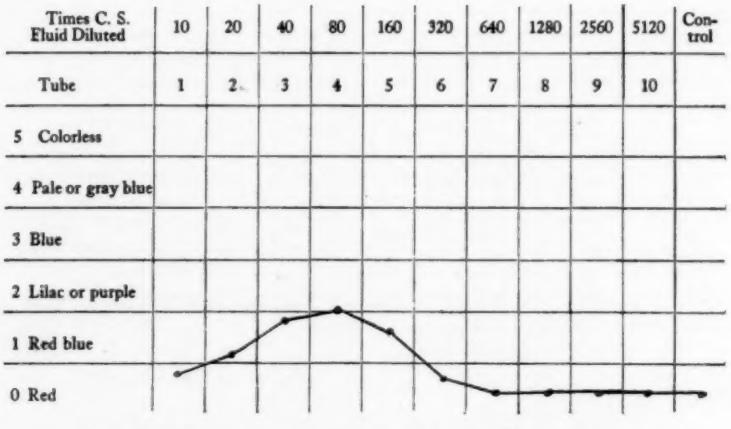

Fig. 3.—Average curve in fourth week of the disease.

cases of poliomyelitis do not present, when they come under observation any increase in cells, or if so, it is little above normal and the globulin may not be augmented. While in other conditions, such as meningismus or tuberculous meningitis, there may be an increase in globulin, as in the former, or an increase in globulin and cells, as in the latter. Hence, positive or negative findings in the spinal fluid as regards cytology or chemistry cannot be considered in the least conclusive. Especially is this the case if poliomyelitis is sporadic and the type atypical, presenting itself in one of its less common forms, such as the meningitic, encephalitic, ataxic, polyneuritic or abortive varieties, or in those cases in which it occurs as a Landry's paralysis, or in which a facial palsy may be the only paralytic involvement present. In such circumstances we need a finer laboratory test to establish the diagnosis, and we believe this is fulfilled by the gold chlorid reaction.

Analysis of Cases as to Presence of Paralysis on Admission and on Discharge, and Degree of Colloidal Gold Reaction

Case No.	Date Admitted to Hospital	Days Ill on Admission	Type of Disease	Paralysis on Admission	Degree of Polyneuritis	Dates of Spinal Fluid Examination	Colloidal Gold Reaction	Paralysis on Discharge	Polyneuritis on Discharge	Degree of Improvement	Recovered or Died
1900	9/26	20	Myelitic, polyneuritic, bulbar	Left arm, complete; legs, complete; back, complete; cranial nerves, involved	2+	10/ 5 10/15 10/29 11/ 5 11/17 12/ 8 1/ 5	1 2 1 1 0 0 0 0 0 0 1 1½1 1 0 0 0 0 0 0 1 1 2 0½0 0 0 0 0 0 0 1 2 2 0½0 0 0 0 0 1 2 1 0 0 0 0 0 0 0 1 2 2 1 1 0 0 0 0 0 2 3 2 1 0 0 0 0 0 0	Right leg, complete; left leg, partial; back, complete; cranial nerves, involved	1+	Slight	Recovered
561	2/18	4	Myelitic, polyneuritic	Legs and neck, complete....	3+	3/ 1 4/18	1 1 2 3 2 1 1 0 0 0 1 1 2 2 0½0 0 0 0 0	Right leg, complete; left leg, partial; back, complete	2+	Slight	Recovered
1901	9/29	8	Myelitic	Right leg, partial.....	—	10/ 7 10/14 10/28 11/ 4 11/11	0 0 1 2 0½0 0 0 0 0 0 0 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	None.....	—	Moderate	Recovered
2196	11/ 6	12	Myelitic, polyneuritic, bulbar	Legs, complete; diaphragm, weak; back, complete; cranial nerves, involved	3+	12/ 2	1½2½2 1 0 0 0 0 0 0	Legs and back, complete; cranial nerves, involved	2+	Slight	Recovered
2005	10/ 2	6	Myelitic	Legs, partial.....	—	10/15 10/30 11/ 5 11/15	1 1 2 2 1 1 0 0 0 0 1 1 2 1 0 0 0 0 0 0 0 1½2 1 0 0 0 0 0 0 1 1 2 1 1 0 0 0 0 0	Legs, weak.....	—	Moderate	Recovered
2130	10/24	2	Meningitic	None.....	—	10/25 11/ 8 11/23	1 2 2½2 0 0 0 0 0 0 0 1 2 2½1 0 0 0 0 0 0½0½2 2 1 0 0 0 0 0	None.....	—	Marked	Recovered
1987	9/28	4	Myelitic, polyneuritic	Legs and back, complete....	2+	9/30 10/21 10/28 11/ 4	0 0 2 3 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Right leg, partial.....	—	Marked	Recovered
1929	9/16	4	Myelitic, polyneuritic	Right arm, weak; legs, weak; back, weak	2+	9/22 10/ 3 10/14 10/29 11/11 11/22	1 1 2 2½3 2 1 0 0 0 0½1½2 2 1 0 0 0 0 0 0 0 1 2 1 0 0 0 0 0 0½1½1 0½0 0 0 0 0 0 1½1½2 3 3 2 0 0 0 0 1 1 2 2½1 0 0 0 0 0	None.....	2+	Marked	Recovered
1011	10/ 4	9	Myelitic, polyneuritic, meningitic	Legs, partial.....	3+	10/ 6 10/12 10/21 11/ 4 11/11 11/21	0½1 2 3 2 2 1 0 0 0 0½0½0½1 2 2 0 0 0 0 0½1 2 2 2 0 0 0 0 0 0 1 1 2 2½2 1 0 0 0 1 2 2 3 0 0 0 0 0 0 1 1½1½2 1 1 0 0 0 0	Left leg, partial.....	2+	Marked	Recovered

2266	11/18	2	Meningitic,	.....	2+	11/24 12/ 2 12/ 8	0 0 1 2 2 1 0 0 0 0 0½1 2 2 1 0 0 0 0 0 0 1 2 2 1½0 0 0 0 0	Legs, weak.....	2+	Moderate	Recovered
1895	9/ 6	4	Myelitic, meningitic, polyneuritic	Right arm and legs, partial; back and neck, weak; cranial nerves, involved	2+	9/20 11/ 5 11/ 8	1 2 2 3 2 1 0 0 0 0 1½2 3 2 2 1 0 0 0 0 1 2 2½2 2 1 0 0 0 0	Right arm, weak; right leg, partial; cranial nerves, involved	Moderate	Moderate	Recovered
2113	10/21	3	Myelitic, polyneuritic	Right leg, partial.....	2+	11/ 2 11/24	0½0½1 2 2½1½0 0 0 0 1 2 2 2 3 2 0 0 0 0	Left leg, weak.....	None	Moderate	Recovered
2019	10/ 5	7	Myelitic	Right leg, partial.....	2+	10/ 6 10/14 10/28 11/ 8 11/12 11/21	0½1 2 2 1 0 0 0 0 0 0½2 1½1 0 0 0 0 0 0 0 0 0½1 0½0 0 0 0 0 0 1 2 1 1 0 0 0 0 0 1 2 2 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	None.....	None	Marked	Recovered
2320	11/26	7	Myelitic, polyneuritic	Legs, complete; back and neck, weak	3+	11/27 12/ 4 1/ 5	0½1 1½2 2 1 0 0 0 0 1½1½2 3 3 2 0 0 0 0 0 2 2 1 0 0 0 0 0 0	Right leg, weak; left leg, partial	None	Moderate	Recovered
1840	8/24	4	Myelitic, polyneuritic, bulbar	Arms and legs, complete; diaphragm and intercostals, weak; back and neck, complete; cranial nerves, involved	3+	10/21 10/28 11/ 5	0 1 1 3 1 0 0 0 0 0 0 0½2 2½3 1 0 0 0 0 1 2 2½2 1 0 0 0 0 0	Arms, partial; legs, complete; back and neck, complete; diaphragm and intercostal, weak; cranial nerves, complete	Moderate	Slight	Recovered
2035	10/ 7	8	Myelitic, polyneuritic	Legs, weak; back and neck, weak	3+	10/28	0 1 2 2 2 1 0 0 0 0	.....	.....	Moderate	Recovered of polymyelitis
2044	10/ 9	5	Myelitic, bulbar	Arms and legs, complete; diaphragm and intercostals, weak; back and neck, complete	1+	10/12 10/21 11/11 11/24 12/ 2	1 1 2 3 3 1 0 0 0 0 1 1 2 3 2 0 0 0 0 0 2 3 3 3 1 0 0 0 0 0 1 2 3 2 1 0 0 0 0 0 0½1½1½1½1 0 0 0 0 0	Arms, partial; legs, partial; back and neck weak	Moderate	Moderate	Recovered
2273	11/19	2	Myelitic, polyneuritic, bulbar	Left leg, diaphragm, intercostals and neck, partial; cranial nerves, involved	1+	11/20	0 0 1 2½1½1 0 0 0 0	.....	.....	.....	Died, 11/21
2229	11/11	4	Ascending Landry's	Left arm and legs, complete; diaphragm and intercostals, partial; neck and back, weak; cranial nerves, involved	—	11/12 11/16 11/17	1 2½2½2 2 1 0 0 0 0 1½2 3 2 1 0 0 0 0 0 1 1 1 2 3 2 0 0 0 0	.....	.....	.....	Died, 11/19
2226	11/11	4	Myelitic, bulbar	Left arm and legs, complete; diaphragm and intercostals, partial; neck and back, partial; cranial nerves, complete	1+	11/13 11/18	1 1 2 1 0 0 0 0 0 0 1 1 2 3 3 1 0 0 0 0	.....	.....	.....	Died, 11/18
2230	11/11	2	Myelitic, meningitic, bulbar	Arms and legs, complete; diaphragm and intercostals, partial; neck, complete	1+	11/12	1 2 3 3 2 1 0 0 0 0	.....	.....	.....	Died, 11/13

In order to show the differential value of the curve obtained in the early weeks of the disease, we have placed in Figure 6 all reactions found during the first ten days or in what might be termed the very acute febrile stage. This, then, forms by its limitations what might be termed for descriptive purposes a poliomyelitic zone. It has been cross sectioned and is thus represented in the figure, and for comparison we have included the curves of various other well recognized meningeal conditions. The figure shows clearly that the zone of Heine-Medin's disease, as made out in this small series, is not identical with that of any other disease.

It is true, that a number of curves are obtained in cases of cerebrospinal syphilis which run a low course, and in which there may be a close resemblance to a poliomyelitic reduction. But while such cases occur not infrequently, the clinical history and symptoms of the two diseases are so different that confusion is entirely improbable. The Wassermann test is moreover, available.

A typical curve of tuberculous meningitis would not be confused with any of our poliomyelitis curves. We have purposely selected as an example of a tuberculous meningitis curve for Figure 6 one which is of as mild a type as was obtainable and one which resembled as much as any which are ordinarily encountered the curve of Heine-Medin's disease. Yet even here the distinction is definite and clear cut, so far as the acute febrile stage of poliomyelitis is concerned. In tuberculous meningitis the curve begins to rise in higher dilutions, not lower commonly than 1:40, and is prolonged well into the meningeal zone in the vast majority of instances, rarely falling below the lilac purple in a dilution less than 1:640.

It must be stated, however, that occasionally one encounters cases, usually those with either marked polyneuritic or meningitic symptoms, in which the gold chlorid curve toward the end of the second week is prolonged slightly beyond the limits of the poliomyelitis zone (Cases 1929 and 1011). Obviously at this period of the disease the question of a differential diagnosis from tuberculous meningitis would not arise.

It must always be kept in mind that if a curve is obtained which transgresses definitely on the meningeal zone, tuberculous meningitis should be ruled out carefully, as the results of our work and that of the majority of our predecessors seem to show that such a reaction is altogether exceptional in the very acute stage of epidemic poliomyelitis.

The colloidal gold reaction is rarely required in the differential diagnosis of poliomyelitis and epidemic cerebrospinal meningitis or any other form of purulent meningitis owing to the entirely different macroscopic, cytologic and chemical characteristics of the spinal fluids in the two diseases. It is possible that in early cases the test might have to be invoked in so much as that in the preparalytic stage of

Heine Medin's disease the cell count is sometimes so augmented as to give a faint hazy appearance to the fluid, while, on the other hand, in the very early stage of epidemic meningitis the fluid may be almost clear, or have a faint opalescence. From Figure 6 it is evident how distinctly different the curves are in the two maladies

As previous work has shown, Lange's colloidal gold test provides the only certain method of differentiating poliomyelitis, and the various forms of meningismus. It was not uncommon during the 1916 epidemic to see cases in which a diagnosis of Heine-Medin's disease had been made in cases which were not such. Thus, occasionally, cases of scurvy, rickets, tetany, etc. were so diagnosed, and, still more commonly, cases of meningismus complicating diverse conditions such as bronchopneumonia, gastro-enteritis or colitis were confused with poliomyelitis. A negative spinal fluid did not absolutely exclude

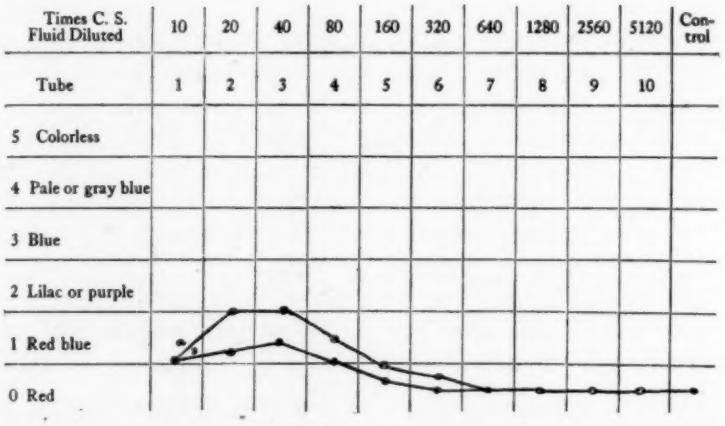

Fig. 4.—Average curve in sixth (a) and eighth (b) week of the disease.

poliomyelitis, while a positive fluid, as regards chemistry, did not prove it to be the latter. Had the colloidal gold chlorid test been employed as a routine in such instances there is no doubt the diagnosis would have been determined more accurately and more quickly. We have employed the test in this way in several cases during the past year, and in no instance did we obtain a reduction of colloidal gold in meningismus. In one case of scarlet fever and poliomyelitis (Case 2266), the diagnosis on admission was meningismus complicating scarlet fever, and we should not have recognized the fact that a mixed infection with the two diseases existed until a later period, after paralysis was definitely manifest, if it had not been for this test. In another patient (Case 24), in whom the physical signs of pneumonia were late in appearing, but who presented a pronounced meningeal syndrome including spastic paralysis of the left arm and leg, due to a lesion in the

course of the upper motor neuron, we were able to rule out Heine-Medin's disease in this way.

As to the value of the colloidal gold test in differentiating poliomyelitis and epidemic encephalitis, the literature gives no information. There has been relatively little work carried out on the use of this test in epidemic encephalitis. Among the few reports made on the subject are those of Tilney and Howe,[10] Davis and Kraus,[11] and Nixon and Sweetser.[12]

Tilney and Howe state that in the greater proportion of cases reported the spinal fluid has been normal and that the colloidal gold curve in the few cases in which it has been studied has been negative. In their case reports are included five cases in which colloidal gold reactions were performed. In three instances the test was negative, and in the remaining two the findings were 1223432100 and 11½22 1½00000.

David and Kraus reported thirty-four cases of epidemic encephalitis, in which forty-three examinations of the spinal fluid were made with the colloidal gold test. Nineteen were in the first three weeks of the disease. Fourteen spinal fluids were absolutely negative; in the remaining five cases the results were as follows: 1112100000; 0000110000; 0001210000; 0012231000; 1122100000. Of the fluids twenty-four taken in the later weeks of the disease, from the fourth to the sixteenth, negative results were obtained in ten, the remaining positive reactions being extremely variable.

Nixon and Sweetser, in an examination of ten spinal fluids obtained from five patients with encephalitis, found the colloidal gold curves exceedingly variable, as follows:

1	2	2	1	1	1	2	0	0		5	5	4	3	3	3	3	2	0
0	0	0	1	1	2	1	0	0		1	1	3	3	3	2	1	0	0
0	0	1	1	1	0	0	0	0		1	1	3	4	4	3	2	1	0
0	0	1	1	1	0	0	0	0		0	1	1	3	3	3	2	1	0
1	2	2	4	4	4	3	3	0		0	0	1	1	2	0	0	1	0

One of us has had five cases of epidemic encephalitis come under his observation and the curves in these cases were as follows:

0	1	1	1	1	0	0	0	0	0	½	1	1	1	½	0	0	0	0	0
0	0	1	1	1	1	0	0	0	0	0	1	1	½	2	1	⅓	½	0	0
1	1	½	1	½	1	½	1	0	0	0	1	2	2	2	1	0	0	0	0

It seems, therefore, that tentatively we may conclude that in a considerable proportion of cases of epidemic encephalitis, there is a negative colloidal gold chlorid curve, while in the remainder of cases in which a

10. Tilney, F., and Howe, H. L.: Epidemic Encephalitis, New York, 1920, p. 105.
11. Davis, T. K., and Kraus, W. M.: Am. J. M. Sc. **161**:109 (Jan.) 1921.
12. Nixon, C. E., and Sweetser, T. H.: Am. J. M. Sc. **161**:845 (June) 1921.

reduction occurs, the reaction is extremely variable sometimes presenting a tabetic, at others a paretic, meningitic, and at times a syphilitic curve. Judging by available information, therefore, only a small percentage of the curves of epidemic encephalitis fall entirely within the "poliomyelitic zone." Accordingly, it may be stated that while a mild syphilitic curve may indicate either one of the two diseases, a negative reaction, a paretic or meningitic curve, would be very strongly indicative of epidemic encephalitis, and as these latter are the usual reactions encountered, the test should be of distinct value in most questionable cases of differential diagnosis.

To realize the full value of this reaction in the diagnosis of poliomyelitis it must be taken into consideration with the history, physical findings and other laboratory data, in each case. It is a laboratory test and as such is subject to a personal equasion of possible error, and it would

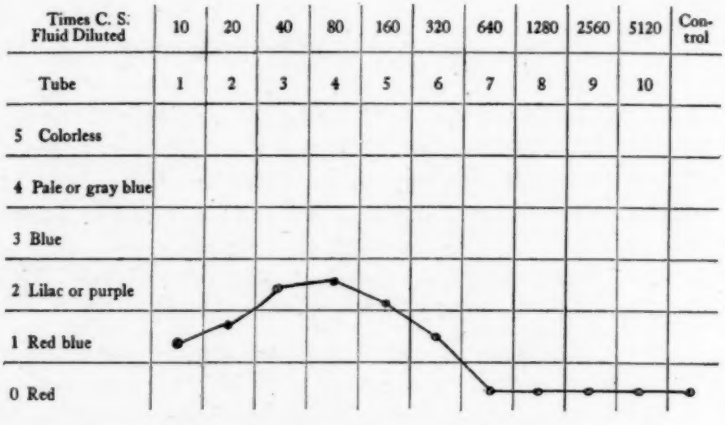

Fig. 5.—Average curve in fatal cases.

be poor policy to rely on it alone to the exclusion of all other information. We must recognize, however, that with a spinal fluid properly collected and preserved and with the test carefully performed by one familiar and experienced with the reaction, it is the most valuable laboratory means we possess at the present time, for the recognition of Heine-Medin's disease.

SUMMARY

The colloidal gold test was performed on seventy-four spinal fluids obtained from twenty-one cases of acute epidemic poliomyelitis. The fluids were examined at intervals varying from the fourth to the one hundred and twenty-third day of the disease. The predominant type of the malady was the myelitic with, however, a high proportion of

cases presenting symptoms of moderate or marked polyneuritis. The curves obtained have been classified according to the week of the disease in which the spinal fluids were taken. On this basis, an average curve has been constructed for each week from the first to the eighth (Figs. 1 to 4). Likewise, an average curve has been prepared from the reactions obtained in the fatal cases (Fig. 5). Finally, in Figure 6, we have placed all the curves obtained in the very acute stage of the disease, and have constructed by their limitations what might be called a poliomyelitic zone. For comparative study the curves of other well recognized meningeal conditions have been placed in the same figure.

CONCLUSIONS

We have drawn the following conclusions from a study of the colloidal gold reaction in this series of cases.

1. There was always a reaction with colloidal gold solution in the case of every poliomyelitic fluid examined during the acute stage of the malady. This reaction was constantly in the same zone (syphilitic zone).

2. The average curves for the first and second weeks of the disease were very similar, and consisted in a gradually rising curve presenting a graduated increase in reduction in ascending dilutions of the spinal fluid, starting in the reddish blue area in 1 : 10, extending into the lilac or purple in 1 : 40 to 1 : 80, and then descending somewhat more abruptly into the reddish blue again in 1 : 160 and reaching the non-reducing or red color in 1 : 640.

3. In the latter weeks of the disease the average curve gradually subsided, reaching normal in a minor proportion of the cases (three out of ten) by the eighth or ninth week, while in the remaining seven (70 per cent.) cases the curve remained still elevated at the ninth week. In two cases examined later than the eleventh week, one in the fourteenth and the other in the eighteenth, the curve was still elevated in both.

4. We have found a fairly typical poliomyelitis curve present in one chronic case as late as five years after the initial attack. This patient had a history of several relapses.

5. Of the three cases in our series, in which the curve reached normal before the end of the eighth week, this ocurred on the twenty-eighth, fifty-third and fifty-fifth day, respectively. It is, therefore, exceptional for the reaction to become normal before the end of the fourth week of the disease.

6. When the curve has once reached normal, it has not been elevated again in the three cases in which this was determined.

7. Cases presenting a persistence of the very acute curve of the first few weeks up into the ninth week or beyond, commonly present at this time either considerable residual paralysis with slight, moderate or marked polyneuritis, or else slight paralysis with a polyneuritis, which still is or has been very marked. A definite persistence of the acute hydrocephalus commonly remains in these cases.

8. We are strongly inclined to believe that there is a relationship between the duration of the positive colloidal gold curve and the acute inflammatory stage of the malady, so that when the reduction of gold chlorid becomes normal, the acute period of the disease is over. If this is so, the reaction should be of value in determining when the rest of the acute period may be terminated, and the more energetic treatment by electricity and massage, etc., of the subacute stage begun.

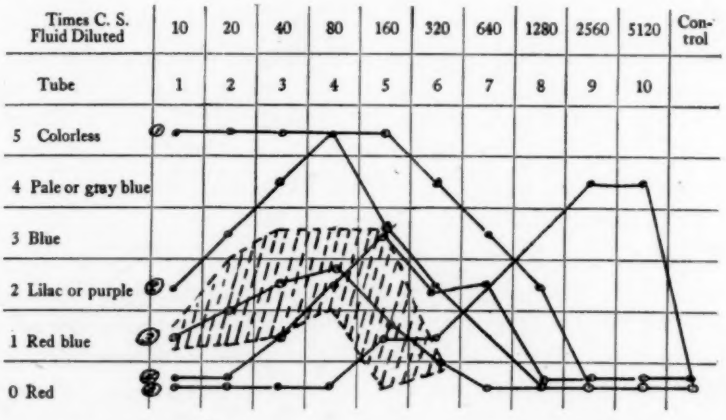

Fig. 6.—Comparative curve in (1) general paresis; (2) cerebrospinal syphilis; (3) Heine-Medin's disease; (4) tuberculous meningitis, and (5) epidemic cerebrospinal meningitis.

9. With the gradual subsidence of the colloidal gold curve there is usually a corresponding improvement in the patient's general condition, paralysis and meningeal symptoms. This relationship does not always hold true, and in patients who have had a marked polyneuritis, the curve may remain acutely elevated in the late weeks of the disease, despite the fact that the paralysis may have subsided entirely.

10. We found no close relationship, except in a general way, between the cytology and chemistry of the spinal fluid and the gold chlorid reaction. As the very acute symptoms subsided, the spinal fluid, in its chemical and cytologic contents, returned to normal. So, in most cases, does the gold chlorid curve return to normal, but more slowly, usually still remaining elevated at a period (eighth week) when

no other characteristic pathologic signs are to be found in the cerebrospinal fluid.

11. The average curve in the fatal cases, although showing a tendency to produce greater reduction, and to be prolonged slightly into the higher dilutions, did not differ sufficiently from that obtained in the nonfatal cases in the first few weeks, as to make the test of value in prognosis.

12. The gold chlorid curve began to fall in a few cases in the third and fourth week, and then was more elevated again in the ninth, tenth and eleventh weeks.

13. The reduction obtained in cerebrospinal syphilis will not usually be confused with that of poliomyelitis, except in a minor proportion of cases in which it runs rather low. In such instances the history and symptoms are so different as to cause no confusion in diagnosis, and the Wassermann test is available.

14. Typical curves of tuberculous meningitis should not be confused with those of poliomyelitis. Even the more unusual types of tuberculous meningitis curves rarely fall entirely within the poliomyelitis zone. If a curve is obtained from a clear fluid of a suscepted poliomyelitis which is prolonged into the meningeal zone, a possible tuberculous meningitis should always be ruled out.

15. In the few instances in which poliomyelitis may be confused with epidemic encephalitis, the colloidal gold reaction may be of some use in differential diagnosis. The reaction in epidemic encephalitis is extremely variable, and a considerable proportion of cases present no reduction at all, while others yield a paretic, meningitic, tabetic or a very mild syphilitic curve. Often the latter two types (tabetic or luetic) fall entirely within the poliomyelitis zone. Hence we may say that in a given case, while such reactions may indicate either of the two diseases, any other type of reduction would point strongly to epidemic encephalitis. It would seem that the difference in reaction to gold chlorid is another point against the identity of the two infections.

16. Lange's reaction clearly differentiated in our series, the various forms of meningismus encountered from Heine-Medin's disease.

17. To realize the full value of this reaction, it must be taken into consideration with the history, physical findings and other laboratory data. We believe, however, that with a spinal fluid properly collected and preserved, and with the test correctly performed, it is the most valuable laboratory method we possess for the recognition of poliomyelitis, especially when the latter disease is sporadic or the type of case atypical.

The writers are indebted to Dr. W. W. Hala, Pathologist, Kings County Hospital, and Mr. F. J. Yonker, of the laboratory staff, for their generous cooperation in the laboratory portion of the work. Acknowledgment is made to Miss Meyers of laboratory staff and also Dr. S. Brody of the intern staff, Kingston Avenue Hospital, for assistance in the laboratory and clinical portion of the work.

THE CLINICAL VALUE OF INTRAPERITONEAL INJECTIONS OF SALT SOLUTION*

J. CLAXTON GITTINGS, M.D., AND JOHN D. DONNELLY, M.D.
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Since the publication of the paper by Blackfan and Maxcy,[1] citing the advantages of the intraperitoneal route for the administration of saline solution to dehydrated infants, the method has been adopted widely and would appear to be one of the most valuable therapeutic procedures which has been proposed in recent years.

In 1914, Dandy and Rowntree injected solutions of phenolsulphonephthalein into the peritoneal cavities of dogs and found that the dye appeared in the blood in from two to four minutes and in the urine in from four to six minutes while the quantitative output in the urine during the first hour amounted to from 40 to 60 per cent. of the amount of dye injected (0.6 mg.) This is fully as much of the dye on the average as is excreted after intramuscular injection and almost as much as though it had been injected intravenously. The result would suggest that absorption of isotonic solutions from the peritoneal cavity is so rapid as almost to equal the efficacy of intravenous injections.

In August, 1919, we began a study to make comparisons between various methods of administering water and to collect statistics on the intraperitoneal method. We first proved at necropsy that it was practically impossible to perforate the bowel by the sudden insertion of a needle through the abdominal wall, and that the peritoneal cavity of guinea-pigs could be injected repeatedly with isotonic salt solution, with or without dyes, without causing harm or discomfort.

In the comparison of different methods of introducing water, the five usual routes were used at first—by mouth, by bowel, intravenously, subcutaneously and by intraperitoneal injection. The first and last soon proved to be the only methods that permit of the safe and painless administration of water in sufficient amounts to be of real value, so that the others were practically discarded so far as the introduction of fluid per se was concerned.

The occurrence of vomiting and the disinclination of the child to drink are the chief practical objections to the oral method of administration. We found that the use of the nasal tube obviated the latter difficulty, and that water, introduced by this method, was retained quite often in spite of the fact that food would be vomited.

* Received for publication, Oct. 12, 1921.

* From the Medical Service of the Children's Hospital, Philadelphia.

1. Blackfan and Maxcy: Am. J. Dis. Child. **15**:19 (Jan.) 1918.

A small, soft rubber catheter (No. 8 to 12 French scale) is lubricated with a stiff grease, such as petrolatum, several drops of liquid petrolatum are instilled into the nostril, and the catheter, with tube and funnel attached, is passed into the esophagus for a distance of from 20 to 25 cm. (from 8 to 10 inches) from the anterior nares. Next, the funnel is held under water. The absence of air bubbles insures that the catheter has not passed into the trachea. From 100 to 250 c.c. (from 3 to 8 ounces) of sterile water are then poured into the funnel. The whole procedure can be carried out so quickly that the water is in the stomach before the child has had much chance to resist. We feel that the introduction of the tube to a point well beyond the epiglottis, but not through the cardia, lessens the incidence of vomiting, and that the nasal route is less apt to induce gagging than is the passage of the tube by mouth. In 80 per cent. of the patients this use of the nasal tube did not excite vomiting at all—or at most, only occasionally. For example, one patient vomited only once during thirty-two treatments and another only twice in thirty-six treatments. Unless vomiting is induced, there is no shock and the discomfort is minimal. Free lubrication is essential when the tube is to be used often.

From 300 to 750 c.c. (from 10 to 24 ounces) of water in twenty-four hours can be administered without any interference with the taking of food, if a four-hour feeding interval is adopted and the water given from three to three and one half hours after a feeding. Many of our "tube" cases also received intraperitoneal injections of saline solution. By the early administration of water by nasal tube to patients with diarrhea it appeared that dehydration sometimes could be prevented.

Ohlmann's results [2] from the administration of water to thirty-four fasting infants and twenty children are of interest in this connection. Using from 200 to 400 c.c. water and collecting the urine at intervals thereafter, he found that infants less than 9 months old voided only from 69 to 92 per cent. of urine in proportion to the water ingested, whereas older children voided from 113 to 175 per cent. This would suggest that dehydration in infants can be influenced quite readily by water administered per oram but that diuresis would be proportionately less active.

INTRAPERITONEAL INJECTIONS

The description of the technic of this proceedure need not be repeated. Marked abdominal distension appears to be the only contraindication. Efforts to relieve meteorism usually were sufficiently successful to enable us, in time, to inject any child who needed it.

2. Ohlmann: Ztschr. f. Kinderh. **26**:291 (Oct. 8) 1920.

As a general rule, we were able to inject from 20 to 30 c.c. (from 5 to 8 fluid drams) for each 480 gm. (pound) of body weight, into infants under one year of age. At times much more than this proportion was injected, but 300 c.c. appears to be a maximum. The needle was withdrawn at once whenever disturbance of pulse or respiration occurred. Occasionally a temperature reaction was observed within three hours, which quickly subsided, except in the event that it merged into the pre-agonal rise seen in some of the desperately ill patients. It is impossible to believe that the injection itself caused these fatalities. Occasionally, there would be a leak of solution through the puncture wound after the needle had been withdrawn. This was usually checked by firm pressure for a few minutes or by a sterile gauze and collodion dressing. In one instance the leak continued for twelve hours, requiring frequent changes of a sterile dressing, but without any serious consequences. Apparently this was due to the use of too large a needle.

In a few cases glucose in 5 per cent. solution was injected in place of saline solution, but this was followed, at times, by such distress and peritoneal irritation, with rise of temperature, as to lead us to abandon its use.

The majority of the cases belonged to the group of gastro-intestinal disturbances with diarrhea. Fifty-seven patients had been acutely ill two weeks or less before admission to the hospital, and twenty-two had been ill more than two weeks. Most of these seventy-nine cases showed more or less intoxication. The mortality was 64.5 per cent. Twenty-six cases were diagnosed infantile atrophy but more or less diarrhea was present. The mortality among these was 61.6 per cent. Two premature infants and one with double otitis media and diarrhea died. Seven infants admitted for regulation of feeding on account of diarrhea and one with pyelitis recovered.

The 116 patients received 352 intraperitoneal injections of physiologic solution of sodium chlorid. The actual amount of fluid injected in the different weight groups shows a relatively larger amount for the youngest children. This can be seen by referring to Chart 1 in which it is shown that the infants weighing between 2 and 3 kilos (average, 2½ kilos) received more than one half the amount given to those who weighed from 4 to 5 or even from 5 to 6 kilos. It is conceivable that we not only met but exceeded the fluid requirements of the small babies.

Comparison Between the Number of Injections and the Mortality.—Chart 2 shows, in general, a rise in the death rate as the number of injections given in each case increases—this, in spite of the fact that in the first two groups, members of which received only one or two injections, we included the desperately ill patients who succumbed within forty-eight hours after admission. It suggests either that water

alone cannot save the more chronic types or that the exhibition of water carries into the "chronic class" some patients who would have died earlier without it. A third explanation might be advanced that the intraperitoneal injections were harmful per se. This is negatived by the experience in individual cases. For example:

H. L., aged 19 months, had been ill with ileocolitis ten days; weight, 9,772 gm. (21½ pounds).

From September 16 to October 19, he received eighteen intraperitoneal injections, during which time his weight fell to 7,366 gm. (16⅕ pounds). In addition to the injections he received glucose, glucose and acacia and physiologic solution of sodium chlorid intravenously. On discharge in December he had almost regained his original weight. None of those who saw him doubted that he owed his recovery to the injections, since his diarrhea and vomiting were so severe as to prevent his retaining any nourishment or fluid for days at a time.

J. T., aged 4 months, had been ill since birth. She was a markedly dehydrated infant with acute diarrhea. Admission weight, 3,864 gm. (8½ pounds).

From November 22 until December 6 she received eight intraperitoneal injections, regaining her admission weight on the latter date.

TABLE 1.—Comparison of Mortality with Total Gain, Loss or Stationary Weight* During Period of Injections

	Number Patients	Recovered	Died	Mortality, per Cent.	Mortality, per Cent. Groups I and II Combined
Gain in weight	33	18	15	45	50
Stationary weight	11	4	7	63	
Lost weight	41	13	28	68.3	

* Weight taken 24 hours after last injection.

Comparison of the Weight with the Mortality.—Table 1 shows the weight taken twenty-four hours after the last injection, compared with the weight on admission, and the mortality. As most of the injections were given daily until the patient was out of danger or moribund, the gain in weight represents, in large part, the increment afforded by water per se as well as the ability of the patient to retain the fluid. The mortality of 50 per cent. in patients whose weight was stationary or had increased, and 68.3 per cent. in those who had lost weight corresponds quite closely to the results obtained in McLean and Lang's cases.[3]

Comparison Between the Number of Stools and the Mortality.—The serious results of the continuance of diarrhea scarcely need any emphasis but the graphic picture presented in Chart 3 gives a visualization which would seem to have some value in prognosis. When the stools continue to average six or more in twenty-four hours after the

3. McLean. S., and Lang, C. A.: Am. J. Dis. Child. **19**:359 (May) 1920.

patient is admitted to the hospital and properly cared for, a very high percentage of fatalities may be expected.

DISCUSSION

The total mortality in the hospital among the 116 patients was 60.3 per cent. Every patient discharged as "recovered" left the hospital in good condition. Cases recorded on the history as "unimproved" were not included in this series.

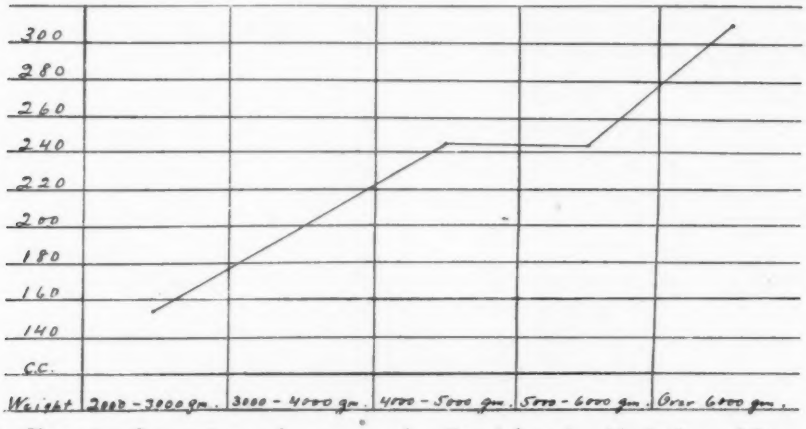

Chart 1.—Comparison of amount of saline injected with body weight.

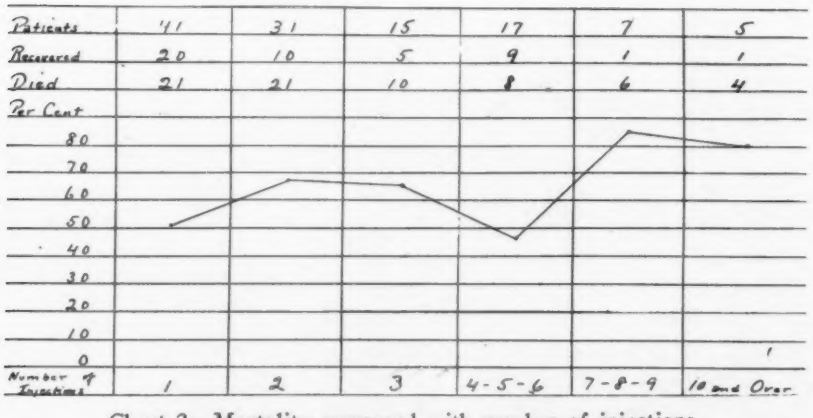

Chart 2.—Mortality compared with number of injections.

The method used for determining the degree of dehydration was purely clinical, based on the elasticity and resiliency of the normal skin and subcutaneous tissues. When these are pinched into a fold, they resume their previous shape and location as soon as they are released from the fingers. The delay in the time of this return which

is seen when the skin of dehydrated infants is pinched, we recorded as one, two or three plus dehydration, depending on the degree. Comparing the degrees of dehydration recorded at the beginning of treatment, with the mortality, we find that in cases showing 3 plus dehydration the mortality was 70 per cent.; in cases showing 2 plus dehydration, the mortality was 60 per cent., and in cases showing 1 plus dehydration, the mortality was 51 per cent. Among the forty-six patients who recovered, thirty-five showed complete return of normal resiliency of the skin, in six the end-result was not stated and in five the dehydration on discharge was recorded as 1 plus, having improved from 2 or

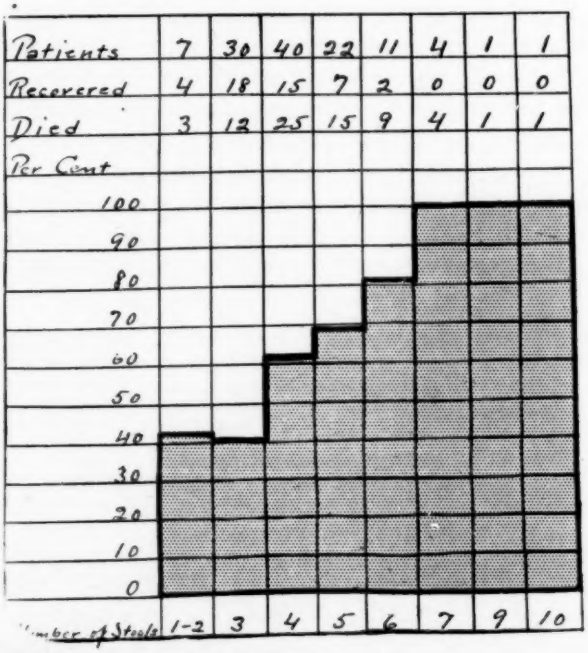

Chart 3.—Mortality compared with average number of stools during illness in the hospital.

3 plus. Among the seventy fatalities the notes on dehydration at the time of death showed: Dehydration same as on admission, 30 cases; dehydration more than on admission, 14 cases; dehydration less than on admission, 19 cases; dehydration entirely relieved, 5 cases; dehydration end-result not stated, 2 cases.

The factor of personal equation in such an empirical method of determining dehydration makes for considerable error but these results confirm the fact that can be demonstrated accurately by a study of blood volume, refractive index, etc., that relief of the anhydremia alone will not cure the worst types.

Necropsies.—In nine of the fatal cases the total of injections was twenty-eight (fourteen in one case), and the necropsy showed that no injury had been done to the peritoneum or to any of the abdominal organs or structures. In seven of the nine cases, in which death had occurred from twelve hours to seven days after the last injection, the peritoneal cavity contained no fluid. In one patient, who had died four hours after receiving 150 c.c. of fluid, the peritoneal cavity contained about 10 c.c. of clear straw colored fluid. In another patient, who died from twelve to twenty-four hours after receiving 500 c.c. of fluid, about 250 c.c. of fluid was found.

Comparison of Results in 1919 with Those in 1920.—The mortality was 81 per cent. in 1919 and 48.6 per cent. in 1920. The improvement may have been due, in part, to a difference in the type of cases, as only in the worst cases were intraperitoneal injections made at the beginning of our study. The atmospheric conditions and the methods of feeding were approximately the same in both years. It was believed that the more extensive use of glucose or of glucose with acacia by intravenous injection in 1920 also might have been a possible factor, but it was found that the mortality among twenty-one patients who received such injections was 71 per cent. as compared with the general

TABLE 2.—ANALYSIS OF CASES IN WHICH SALINE SOLUTION WAS INJECTED

	Year	Number Patients	Average Amount Injected, C.c.	Maximum	Minimum
Recovered.....	1919	8	200	450	150
	1920	31	169	315	75
Died.....	1919	34	298	650	100
	1920	34	187	325	100

mortality of 48.6 per cent. Judging from certain individual cases we are inclined to believe, however, that the amount of saline injected intraperitoneally in 1919 often was too large. Excluding nine cases in infants over 1 year of age who received the largest amounts of saline on account of their size, the findings were as shown in Table 2. Averages cannot be accepted as applying to individual cases but the indication is plain that the amounts of fluid injected in 1919 were considerably larger than in 1920. It is our practice at present not to give more than 150 c.c. for babies weighing less than 4 kilos, with 300 c.c. as a maximum.

SUMMARY

The forced ingestion of water by nasal tube deserves a more extensive trial in cases of diarrhea as a preventive, before anhydremia develops, and, in conjunction with intraperitoneal injections, as a curative measure. Other routes for the introduction of water rarely will be needed.

The optimum amount of fluid to be administered by mouth and especially the amount to be injected into the peritoneal cavity, should be determined more accurately. At present we feel that intraperitoneal injections should not exceed 300 c.c. and that 150 c.c. administered more frequently, if necessary, is a safer procedure for infants weighing less than 4,000 gm.

Puncturing the peritoneal cavity seems to be a safe procedure, provided the bladder is empty, distention is not extreme and a rigidly aseptic technic is employed.

There is need for a reliable clinical measure of the degree of dehydration. The lack of resiliency in the skin and subcutaneous tissues seems to give a reasonably accurate indication, but it should be controlled carefully by tests of the blood volume, blood flow and protein concentration.

Dehydration in itself must be an important factor in producing symptoms and in determining the outcome, but it cannot be held solely responsible for the deaths in many of the cases. The bad result of the continuance of diarrhea, however, is as sure now as it was before dehydration was adequately recognized.

HEMATOMAS IN THE HEART VALVES OF CALVES*

LAURA FLORENCE, PH.D.

PRINCETON, N. J.

The presence of hematomas in the heart valves of new-born calves is today a widely known fact. Nevertheless, a survey of veterinary literature reveals only brief references, and, since in these the microscopic structure and possible origin of the hematomas have not been discussed, a study of these two points was undertaken. The literature describing hematomas in the heart valves of children was not consulted until the conclusion of the work on calves.

Kitt [1] describes the hematomas as being bladders of blood or serous fluid, varying in size from a lentil to a pea, situated between the flat endocardial folds of the artioventricular valves, and raised somewhat above the surface of the valve. He gives no references but cites Glage and Kläger, whose observations agree with his own on slaughtered swine and young calves, and Gibson who had seen similar small cysts in lambs. Ostertag [2] refers to the hematomas as true hemorrhages, which he considers normal and not infrequent in young calves. He also cites Kläger. In 1914 Egge [3] published a short paper and in the same year another reference appeared in the textbook of Jost and Koch.[4] The latter add nothing to the description of Kitt. From 1905 to the time of publication, Egge examined the hearts of young calves slaughtered in the abattoirs under his care, and in the heart valves of almost all the animals he found extravasations consisting, in part, of sharply defined swollen blood tumors varying in size from a pinpoint to a pea, and in part of more or less large level areas of blood in the tissue of the valve. These were situated in the region of attachment of the chordae tendinae. He also examined the hearts of fetuses and prematurely born calves with positive results. He did not find hemorrhages in calves that had lived four or five weeks, and concluded that the blood must be absorbed during the first weeks of extra-uterine life. He offers no explanation of the presence of these hemorrhages and refers only to the work of Ostertag. He also examined the hearts of foals, young swine, and lambs, but never found any extravasations.

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* Received for publication, Oct. 17, 1921.

* From the Department of Animal Pathology of The Rockefeller Institute for Medical Research.

1. Kitt, T.: Pathologische Anatomie der Haustiere **2**:310, 1906; Ibid. **2**: 337, 1911.

2. Ostertag, R. von: Handb. d. Fleischbeschau, Stuttgart **1**:263, 1910.

3. Egge, G.: Berl. Tierärtzl. Wchnschr. **4**:63, 1914.

4. Jost, J., and Koch, M.: Krankheiten junger Tiere im Vergleich mit Kinderkrankheiten, 1914, p. 631.

We have been unable to find the original references of Glage, Kläger and Gibson.

Similar hematomas are of frequent occurrence in the heart valves of new-born and young children, and they have been seen in the human fetus and in still-born children. The literature has been carefully reviewed by Wegelin,[5] consequently only a brief summary is given here. Luschka,[6] who cited Elsässer [7] as the first to mention hematomas in the heart valves, accurately described their macroscopic appearance and attributed their origin to hemorrhage, due to ruptured vessels, into the soft tissue of the noduli albini. Parrot [8] also thought that they were formed through the rupture of intravalvular blood vessels after birth but regarded the noduli albini as resulting from the organization of this hemorrhage. In 1898 Berti [9] published an entirely new view. He discovered the endothelium lining the blood cavities and concluded that they were not hematomas but varicose vessels or blood cysts due to changes in the pre-existing blood vessels. He also examined a number of animal hearts and pictured a cyst in the atrioventricular valve of a four-weeks-old lamb. The same year Haushalter and Thiry [10] described a connective tissue layer and not endothelium surrounding the blood cavities and again named them hematomas. They saw no vessels in the valves in the neighborhood of the hematomas, but in serial sections traced a connection between them and the cavity of the ventricle. They thought the blood was forced into the bays on the under surface of the valve at birth and in earliest infancy, and that the soft tissue gave way before the pressure allowing the blood to penetrate the valve. This blood was then dammed back in the tissue during the ventricular systole through the stretching of the valve and the pull of the chordae tendinae. This view was severely criticized by Berti.[11] Fahr [12] examined the hearts of children during the first months of life and in almost every case found hematomas in the valves. He also found them in most of the fetuses he examined from the sixth month of development. Like Berti [9] he saw the endothelium lining the blood cavities and thought them vessel ectases. Wegelin [5] described the histologic structure in great detail and figured serial sections to demonstrate his theory of the formation of the hematomas. He agreed with Haushalter and Thiry that they were formed by the

5. Wegelin, C.: Frankfurter Ztschr. f. Path. **2**:411, 1909.
6. Luschka, H.: Virchows Arch. f. path. Anat. **11**:144, 1857.
7. Elsässer: Bericht über die Ereignisse in der Gebäranstalt des Catharinenhospitals, Stuttgart, 1844.
8. Parrot, J.: Arch. de physiol. norm. et path. **1**:538, 1874.
9. Berti, G.: Boll. delle sc. med. di Bologna, 1898, pp. 343, 479, 581; Referat, München. med. Wchnschr., 1898.
10. Haushalter, P., et Thiry, Ch.: Arch. de méd. expér. **10**:558, 1898.
11. Berti, G.: Arch. f. Kinderh. **31**:371, 1901.
12. Fahr: Virchows Arch. f. path. Anat. **184**:274, 1906.

forcing of the blood against the valves, but he also recognized the endothelial lining of the cavities and said they arose through the widening and secondary cutting off of some of the bays which lie normally on the ventricular side of the valve where the chordae tendinae are attached. Just after Wegelin had finished his investigation, but before the publication of his results, two further papers appeared. Meinhardt [13] had arrived independently at practically the same conclusions as Wegelin. Hammes [14] also saw the narrow canals connecting the blood cavities with the ventricle, but agreed with Berti in considering the hematomas ectases of true vessels. Also he thought they had no connection with the coronary system but constituted a second type of valve vessel serving to nourish the valves during the last third of fetal life and the first year of extra-uterine life.

During the past five years accumulations of blood have been seen very frequently in the tissues of the atrioventricular valves in the fetuses and young calves examined in this institute. These have not been found in the semilunar valves of calves by us or by Egge, but they have been recorded by a number of pathologists as occurring in these valves in children. As stated by Egge, these accumulations of blood are of two distinct types. There are clearly defined hematomas varying in size from a pinpoint to a large pea; the largest one sectioned had a diameter of 6 mm. They are usually subcircular, but frequently a few very small hematomas are scattered close around the border of the larger ones giving a false appearance of an irregular edge. There may be one or several in a valve, and occasionally we have seen a number of small ones clustered together, resembling somewhat the surface of a blackberry and extending over the greater part of the valve. They are slightly raised above the atrial surface but not so much so as those in children as described by Berti and Wegelin, and are visible from both surfaces of the valve. They are usually blackish-red in color, but sometimes they are bright red. Most are firm to the touch and evidently quite filled with blood, but occasionally some are not fully distended and are soft to the touch, so that their form changes somewhat under pressure. The second type is hemorrhage over a level area of irregular outline and not at all elevated above the surrounding surface; some of these have been found bright red and others blackish-red in the fresh state. In one case of a calf, which died when two days old, hemorrhage extended around the entire set of valves of the right side of the heart, while numerous hematomas were present in the valves of the left side. Both types are situated among the attachments of the chordae tendinae.

13. Meinhardt, H.: Virchows Arch. f. path. Anat. **192**:521, 1908.
14. Hammes, F.: Virchows Arch. f. path. Anat. **193**:238, 1908.

Valves from the hearts of eight calves, varying in age from one day to three months, have been studied microscopically by means of serial sections stained with eosin and methylene blue, hematoxylin and eosin, and by the Gram-Weigert method. The two types of hemorrhage present very distinct pictures. In the case of the hematomas our findings are similar to those of Wegelin, although our interpretation of them is somewhat different. In every case there was a clearly defined cavity lined with a single layer of endothelium and well filled with blood cells among which the mononuclear and polynuclear elements were present in normal numbers. In a few cases in which the cavity was much distended there was crowding of the surrounding tissue which gave a false appearance of a connective tissue capsule. The largest hematomas extended into the region of the muscle at the attached border of the valve. In no case were true blood vessels found communicating with the hematomas, but their connection with surrounding slender endothelial-lined channels and clefts could frequently be traced through successive sections, while at other times chains of endothelial cells with large dark-staining nuclei and a narrow border of cytoplasm were the only trace of original channels. Neighboring hematomas were often seen to become confluent with one another and form large blood-filled cavities which in later sections again divided into small cavities. In children Haushalter and Thiry described the disappearance of the hematomas through destruction of the red cells, accumulations of fibrin, invasion of the blood by round cells, and by budding. Wegelin also saw the hematomas obliterated through the changing of the red cells into a hyalin mass and its subsequent organization by the outgrowth of endothelial and connective tissue cells. In the oldest calves studied, traces of budding of endothelial and connective tissue cells were seen in the hematomas, but never such accumulations of fibrin as Haushalter and Thiry described or the collections of pigment mentioned by them and by Wegelin. These accumulations of blood are either organized or absorbed, since they are not found in older animals.

A study of serial sections of the level areas of blood showed that they were due to an extravasation of blood into the tissue of the valve. Where much blood had escaped the structure of the valve was entirely concealed but in other cases numerous capillaries and clefts were seen. In none of the sections was there any evidence of rupture and the blood had apparently escaped from the vessels by diapedesis. Such a condition, while tolerably frequent in calves, is evidently unusual in children, since Wegelin alone mentioned small hemorrhages under the endothelium and in the tissue surrounding small hematomas. In none of the cases studied have any other pathologic conditions been found in the valves.

In the majority of the calves having blood accumulations in the heart valves punctiform hemorrhages are frequently seen in the alimentary tract, particularly in the fourth stomach and in the pyloric and ileocecal valves and rectum. Their importance, owing to their opening a way of infection, and their possible connection with the hematomas and hemorrhages of the heart valves will be discussed in a later paper.

DISCUSSION

Three different views have been stated concerning the source of the hematomas found in the heart valves of children: first, that they were the result of hemorrhage; second, that they were ectases of true blood vessels; and third, that they were the result of the forcing of blood into the soft tissues of the valve during the ventricular systole. Each view has with various modifications been supported by a number of investigators and both Berti and Wegelin have discussed the question at considerable length. The present study has suggested another origin.

Since hematomas are found only in the valves of fetuses and very young animals their origin must be looked for in the course of the development of the heart. Minot [15] first pointed out that in all vertebrates there occur two types of blood vessels with endothelial walls only, namely, capillaries and a second form which he named sinusoids. The facts of the development of the cardiac trabeculae were already well known, but Minot first interpreted the condition as a sinusoidal circulation and as showing the primitive circulation of the heart itself. Only later when the coronary arteries develop is a true capillary circulation formed. His study of embryos led him to conclude that for a time the nourishment of the heart is direct, from its own contained blood. Lewis [16] confirmed Minot's work and showed both in fish and rabbits that the heart has a superficial capillary and a deep sinusoidal circulation wholly different in their development. In adult fishes and amphibians the sinusoids remain highly developed while in mammals they undergo a regression. According to Lewis many sinusoids are "reduced to strands of endothelium without lumen. Others are retained as slender vessels opening into the ventricle at both ends. These are probably the source of those vessels of Thebesius described by Langer [17] in adult human hearts, as associated with the papillary muscles and communicating at both ends with the ventricle. Other sinusoids remain large, and seem to anastomose with the coronary vessels suggesting the free communication between the ventricles and coronary veins found by Pratt [18] in the heart of calves."

15. Minot, C. S.: Proc. Boston Soc. Nat. Hist. **29**:185, 1900.
16. Lewis, F. I.: Anat. Anz. **25**:261, 1904.
17. Langer, L.: Sitz.-Ber. d. Akad. d. Wiss. Wien. **82**:25, 1881. Quoted by Lewis.[16]
18. Pratt, F. H.: Am. J. Physiol. **1**:86, 1898. Quoted by Lewis.[16]

In the course of their development the anlagen of the valves are connected with the trabeculae of the ventricles. The muscle bundles on the atrial surface of the valve anlagen pass toward the ventricles and are apparently continuous with the ventricular bundles so that for a time the valve cusps consist partly of endocardial growths and partly of musculature. At first the endocardial growths greatly surpass the muscular and later the trabeculae which pass from the spongy substance of the ventricles to the valves increase greatly and the central portions of the valves come to project further into the lumen. The trabeculae separate from the corticalis and pass more toward the center and at the same time the musculature of the valves undergoes considerable development. Later this musculature of the valve is replaced by connective tissue and elastic threads and the trabeculae become transformed into chordae.

During the period of intimate connection between the trabeculae and developing valves the sinusoidal circulation doubtless penetrates and nourishes the latter. It seems reasonable then to infer that the hematomas are vestiges of the primary sinusoidal circulation of the heart, and that the strings of cells, slender vessels, and smaller clefts seen in all sections of valves are also vestiges of sinusoids and, as Lewis suggests, may be the vessels of Thebesius. Among previous workers only Hammes suggested that the hematomas and small vessels might be a distinct circulation apart from the coronary circulation.

In studying serial sections of the true hemorrhages, capillaries and small clefts congested with blood were seen wherever the hemorrhage was not so abundant as to conceal all the structure of the tissue. In successive sections these vessels could not be traced to any connection with larger vessels toward the base of the valve, so it must be inferred that they are some of the vessels of Thebesius and that the hemorrhage has taken place by diapedesis through their walls.

The existence of such an independent innner circulation in the heart may also account for the great variety of opinion as to whether the atrioventricular valves are vascular or not. The most recent work we have seen is that of Argaud.[19] He concluded that in oxen, as in man, blood vessels are sometimes present in the valves, and that in horses they are always present.

Hematomas have not been recorded as occurring in the semilunar valves in animals, and in children much less frequently in these than in the atrioventricular valves. Wegelin considered this to be the result of the small number of invaginations on the surface of the valve and the small quantity of elastic threads in the tissue, while in accordance with our hypothesis it would be due to the great restriction of trabeculae in the atria. In spite of the fact that the small quantities of blood

19. Argaud, R.: Compt rend. Soc. biol. **62**:812, 1912.

invariably present in the bays between the chordae tendinae and communicating with the cavity of the ventricle suggest the formation of the hematomata by the forcing of the blood into deeper bays as Wegelin and Meinhardt have concluded, their interpretation as remains of the primary sinusoidal circulation seems a more natural process.

These cavities filled with blood are not true hematomas, and some writers have suggested that they be called blood cysts. Only a microscopic study of the valves of fetuses at different stages of development will actually prove our hypothesis of their origin as sinusoids and till then we propose to retain the name hematoma.

CONCLUSIONS

Hematomas and hemorrhages are of frequent occurrence in the atrioventricular valves of fetuses and young calves. Both are situated in the region of attachment of the chordae tendinae and may occur in the same valve.

The hematomas are subcircular cavities lined with a single layer of endothelial cells and may be sinusoids which persist from the primary sinusoidal circulation of the heart.

The hemorrhages apparently occur by diapedesis from the vessels of Thebesius.

No other pathologic conditions have been found in the affected valves.

EFFECT OF TONSILLECTOMY ON NUTRITION IN TWELVE HUNDRED CHILDREN *

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Tonsillectomy has become a common operation. The indications for this procedure differ. Until recently tonsils were removed only if they were obstructive or presented definite evidence of infection. Marked improvement followed the removal of such tonsils in most instances. In recent years the operation has been recommended as a prophylactic procedure, and so-called potentially diseased tonsils are removed. Much is expected from a tonsillectomy and I believe rightly so if the tonsils are at fault. One is so often impressed with the marked improvement in nutrition after such an operation that the influence of the operation on nutrition cannot be overlooked.

In a clinic in which ten thousand children were subjected to the operation, a study was made of twelve hundred to determine the effect of the operation on nutrition. These children received more or less uniform care having all been operated on in one clinic by the same surgeons and selected for operation by two physicians who followed a uniform standard for the designation of cases for operation. A careful history was taken of each child, and the definite complaints of the child were charted. All the cases were so-called extreme cases with obviously diseased tonsils and adenoids, or presenting complaints definitely referable to a possible focus in the tonsils. Practically all these children were operated on in the summer of 1920 and reexamined from nine to twelve months later. The estimation of the child's nutrition is based on the height—weight relationship. When the children appeared for operation they were measured in stocking feet and weighed without outside clothing. The same children were similiarly measured and weighed at this subsequent examination. Weights and measurements were compared with the table of average weight and height measurements published by Dr. Emerson for the Nutrition Clinics for delicate children.

The children operated on represented the so-called urgent cases. The reasons for operation varied. Many children had large obstructive tonsils and adenoids, others obviously infected tonsils while a few showed no evidence of diseased tonsils but had recurrent infections in the head which could be attributed to the tonsils. There seemed to be a definite indication for operation in each case.

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* From the Nose and Throat Department of the Rochester Dental Dispensary.

The 1,200 children studied ranged in age from 3 to 15 years. These children presented themselves for operation because of throat symptoms and not because of malnutrition and thus do not represent necessarily a group of malnourished children. No effort was made to place these children in a nutrition class though the school nurse or social service worker had instructed them in habits of life which might have some bearing on their nutritional improvement.

The children were grouped into three classes: (1) Those who were 10 per cent. or more overweight; (2) those who had normal weight or were less than 7 per cent. underweight (so-called borderline cases); (3) those who were 7 per cent. or more underweight. At the time of reexamination the same children were reclassified to determine their nutritional status after the operation.

TABLE 1.—NUTRITIONAL STATUS OF CHILDREN AT TIME OF OPERATION

	10 Per Cent. or More Overweight		Normal Weight or Borderline Cases		7 Per Cent. or More Underweight	
	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
Boys	37	3.1	323	28	185	15
Girls	40	3.9	381	31	224	19
Total	87	7	704	59	409	34

In this group of 1,200 children the percentage of malnutrition (34) was about the same as is being found in the schools throughout the city. Though an equal number of girls and boys were examined, it was noted that malnutrition existed in 4 per cent more girls than boys. The age distribution is not significant. More children were underweight between the ages of 5 and 9 than in later childhood.

TABLE 2.—NUTRITION STATUS OF CHILDREN NINE MONTHS AFTER OPERATION

	10 Per Cent. or More Overweight		Normal Weight or Borderline Cases		7 Per Cent. or More Underweight	
	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
Boys	57	4.7	425	35.5	70	5.9
Girls	67	5.5	461	38.4	120	10
Total	124	10.2	886	73.9	190	15.9

A reexamination of these children from nine to twelve months after the operation showed a marked improvement in the nutrition. Generally, it can be stated that when the nutrition improved, the symptoms for which the child was operated on were relieved. In order to determine the net gain in weight, the growth of the child had to be taken into consideration. The weight was computed for the child's height, measured as at the original examination, and the entire group reclassified. It was found that in the group of 1,200 children the per-

centage of malnutrition, or those who were 7 per cent. or more underweight, was 15.9. In the normal classification were 73.9 per cent. of the group, while 10.2 per cent. were 10 per cent. overweight.

An analysis of the 15.9 per cent. representing 190 children who failed to attain their normal weight shows that other factors besides diseased tonsils are at fault. Englarged cervical glands following tonsillectomy were found in fifteen cases. Pertussis, bronchitis or some other infection, followed the operation in others. Poor home control and improper diet could be traced to others. More careful examinations of this group will need to be made to determine their failure to gain properly.

It is significant, however, that about 50 per cent. of the 409 underweight children should have attained their normal weight for their height in a period of nine months. Without any other efforts to improve their nutrition it seems fair to assume that diseased tonsils and adenoids were at least partly responsible for this condition. It must be stated that not all children improved their status or even held their own, for 7 per cent. of the total number were relatively in poorer nutrition at the time of reexamination that at the time of operation. But of the entire group 219 children showed a very marked nutritional improvement.

TABLE 3.—NUTRITIONAL IMPROVEMENT MADE AFTER OPERATION

	Number Examined	Number Overweight	Number Normal Weight	Number Underweight
At time of operation	1,200	87	704	409
Nine months after operation	1,200	124	886	190

CONCLUSIONS

1. Among 1,200 children operated on for diseased tonsils and adenoids there was 34 per cent. malnutrition (7 per cent. or more underweight).

2. Reexamination from nine to twelve months later showed a reduction of malnutrition to 15.9 per cent.

3. Diseased tonsils and adenoids do not necessarily impair nutrition, as evidenced by 66 per cent. of children showing normal weight according to height.

4. Diseased tonsils and adenoids are undoubtedly a factor in malnutrition, as evidenced by the marked improvement in 219 children of the group.

CLINICAL DEPARTMENT

REPORT OF A CASE OF GANGRENE OF THE FEET FOLLOWING DIPHTHERIA *

MURRAY B. GORDON, M.D., AND BENJAMIN NEWMAN, M.D.
BROOKLYN

Peripheral gangrene following diphtheria is of very rare occurrence. Ker [1] mentions the condition but states that he never saw a case. He refers to Rolleston,[2] who saw a case in 1910 and who was able to collect ten others from the literature at that time. Robbins [3] published a review of twenty-five cases of peripheral gangrene following diphtheria. The next important contribution to the subject was a critical and exhaustive résumé of the literature by Bailey.[4] No new case has been reported since. Our case is the fourth to be observed and reported in America, the previous ones having been published by Vedder (1879), Ward (1894) and Munn (1894).

REPORT OF CASE

History.—Abraham A., 6 years old, gave a history of having had a sore throat for four days without having received any medical attention. On the fourth day, a physician was called. He made a diagnosis of diphtheria and administered 15,000 units of antitoxin and advised removal to a hospital.

Examination.—The boy was admitted to the Kingston Avenue Hospital, April 26, 1920. He was poorly nourished and pale. Eyes and ears were negative. His throat showed an involvement of the fauces and pharynx, the membrane extending over both tonsils, uvula, posterior nares, nasopharynx and the pillars of the soft palate on the left side. Glandular involvement was moderate. The lungs were negative. The heart sounds were of good quality, rapid but no murmurs. The spleen was negative. The liver extended over to the left and could be felt about 2 inches below the free border of the ribs. He was given an additional 25,000 units of antitoxin intramuscularly.

Course.—Seven days after admission, the heart sounds became weaker in muscular tone and irregular. On the next day, he complained of severe pains in the left foot. There was a difference in the temperature between the two lower extremities, the left feeling colder to the touch. Purplish colored ecchy-

* Received for publication, Oct. 28, 1921.

* From the Kingston Avenue Hospital for Contagious Diseases, Department of Health.

1. Ker, C. B.: Infectious Diseases, Oxford University Press, London, Ed. 2, 1920.

2. Rolleston, J. O.: Brit. J. Child. Dis. **7**:529, 1910.

3. Robbins, F.: Juvenile Peripheral Gangrene in Infectious Diseases; Diphtheria, Med. Rec. **94**:620, 1918.

4. Bailey, L.: Occlusion of the Arteries of the Limbs in Diphtheria, Internat. Clin. **2**:157, 1920.

motic areas were irregularly distributed over the skin of the left thigh and leg. These disappeared by the following day but the toes of the left foot seemed to be of a blue color as compared with the pink color of the right foot. The thigh and leg had become somewhat warmer to the touch. Sensation was lost in the lower half of the left leg and foot, and there also was an apparent weakness of the same limb which caused it to hang flaccid. The reflexes were altered, in that the knee jerks were absent on both sides, the plantar reflex was absent on the left but present on the right; ankle clonus was negative on both sides, Oppenheim sign was normal on the right side but no response was elicited on the left; no Babinski or Kernig on either side. The pain in the left leg and foot was severe enough to necessitate the administration of morphin.

Coincidently with these local changes, the heart condition had become progressively worse so that on the twelfth day in the hospital there was a pronounced myocarditis with a gallop rhythm, reduplicated second sound and a tumultuous heart action. There were no murmurs. The throat was clear of any exudate but still gave a positive diphtheria culture. A posterior palatine paralysis with nasal regurgitation of fluids had developed. The child, however, was in an apparently comfortable condition.

Examination of the pulsation in Scarpa's triangle showed that it was present on both sides but not as pronounced on the left side as on the right. The popliteal pulsation was also not as definite on the left side as on the right.

The bluish discoloration of the left foot persisted, this being present on the dorsum and to a lesser extent on the plantar surface, being accompanied by a dilatation of the veins. The foot was swollen and waxy in appearance. The condition ameliorated with the establishment of a collateral circulation so that the foot became warmer to the touch and the color picture changed so that a few days later the dorsum presented two zones. From the ankle to the toes, the color was a deep cyanotic purple of uniform intensity, while just above and around this area was a zone of purplish red hyperemia. The deep purplish hue extended to the plantar surface. The cyanotic zones on both surfaces were swollen, edematous and hard to the touch.

Eight days subsequent to the involvement of the left foot, the boy experienced a sharp pain in the right foot. Within a day or two this was followed by a sensation of cold in the right foot and the appearance of irregularly distributed purplish areas on the dorsum. The foot became swollen. The toes became involved and then the heel. Within a few days, however, the cyanosis of the toes and dorsum of the foot gradually disappeared, but the discoloration on the heel remained, attaining the size of a silver trade dollar. The temperature on the right side gradually became lower than that on the left, especially from the knee down, the foot itself being almost ice cold. The cyanosis was not as pronounced as in the left foot, nor were the two color zones as definite. Within a week after the onset of the process in the right foot, the condition had improved to such an extent that the gangrene was limited to a small portion of the heel.

The process in the left foot became confined to the toes, a small portion of the plantar surface and 2 inches above the metatarsal phalangeal junction on the dorsum, the affected area being of a blackish purple color, hard in consistency and not painful. A sharp line of demarcation formed between this area and a surrounding one of a reddish pink. Within a month subsequent to the onset, the toes of the left foot showed a beginning desiccation, the dry gangrene also including a small portion of the plantar surface and some distance above the toes on the dorsal surface. The gangrene on the right heel was later confined to the skin and a slight area of superficial tissue.

Sloughing of the tissue ensued at the line of demarcation in both feet, resulting in a natural amputation of the gangrenous area in the right heel and a separation of the tissues down to the bone at the metatarsal phalangeal junction in the left foot. This process was permitted to continue for two months until the condition of the child had improved.

PROGRESS IN PEDIATRICS

RÉSUMÉ OF LITERATURE (1920) ON TUBERCULOSIS IN CHILDREN *

MAY MICHAEL, M.D.
CHICAGO

MODE OF INFECTION

J. W. ALLAN [1] is of the opinion that antenatal tuberculosis is more common than is generally believed and that many children are born with "seeds" of the disease lying latent which at a later period of life give rise to manifest tuberculosis. He thinks the placenta offers the most likely portal of entry for the tubercle bacillus, and quotes Bonny, who says that, despite the normal appearance of the fetal organ and of the placenta, tuberculosis has resulted from inoculation of animals with portions of these tissues and with blood from the placental circulation. Allan thinks that to account for the subseqent development of tuberculosis in the animals inoculated these apparently healthy tissues must have contained some "seed" or inverted form of the tubercle bacillus.

M. DUBOIS [2] adds the report of a case of intrauterine tuberculous infection to those already found in the literature. A woman suffering from miliary tuberculosis gave birth, prematurely, to a child. Forty-two days later she died and necropsy showed, besides the miliary tuberculosis, an old caseous tuberculosis of the left tube, of the endometrium, and a diffuse tuberculous peritonitis. The miliary tuberculosis originated either from a large tubercle in the right renal vein or from caseated tubercles found in the wall of the small uterine vessels.

The child, removed at once from the mother, developed poorly and died on the fifty-fourth day. The necropsy showed an old softened lesion in the right upper lobe with caseation of the right bronchial lymph glands, as well as a generalized miliary tuberculosis. The finding in the mother of a tuberculosis of the endometrium, which involved the site of the placenta and the age of the pulmonary and bronchial gland tubercles speak for an intrauterine infection either of hematogenous origin or due to aspiration of the amniotic fluid. The author

* Received for publication Dec. 10, 1921.

1. Allan, J. W.: Prenatal Tuberculosis, Glasgow M. J. **93**:1 (Jan.) 1920.

2. Dubois, M.: Intrauterine Tuberculous Infection, Schweiz. med. Wchnschr. **50**:772 (Aug. 26) 1920.

thinks the latter more probable because of the presence of the oldest lesions in the lung of the child and the findings in the uterus of the mother.

BACTERIOLOGY

A. STANLEY GRIFFITH [3] has tried to ascertain the relative proportion of the human and the bovine types of tubercle bacilli in different kinds of human tuberculosis. Of twelve cases of tuberculous meningitis, ten were caused by the tubercle bacillus of the human type and two by that of the bovine type. In one instance the cow's milk supplied to the patient was found to contain virulent tubercle bacilli, indentical in cultural characteristics with the strain from the meninges of the child.

Of seventeen cases of phthisis, sixteen were caused by the human bacillus and one by the form of bacillus recently found in various kinds of human tuberculosis and in one case of simian tuberculosis. Of twelve miscellaneous cases (three of bone and joint tuberculosis, eight of glandular tuberculosis, one of intermuscular abscess) nine were caused by the human type of bacillus, two by the bovine type, and one by a type which resembled the bovine but differed slightly in cultural characteristics and virulence.

From sixty cases of scrofuloderma, fifty-two cultures of the tubercle bacilli were obtained. Of these, sixteen showed the bovine type of bacillus, four a type less virulent than the ordinary bovine bacillus, and thirty-two the common human type.

The author reports that in England 1,068 cases of tuberculosis have been examined for the type of tubercle bacillus, 803 showed the human type, 194 the bovine, and five a mixed type.

N. NOVICK [4] has studied the incidence of bovine infection in tuberculous meningitis. He quotes Park and Krumwiede, who found 15 per cent. of bovine infection in tuberculous meningitis among 1,000 cases of all forms of tuberculosis, and Rosenau, who analyzed 1,040 cases of tuberculous meningitis, which included those of Park and Krumwiede. Rosenau's figures were as follows: Among 685 patients 16 years of age or over, with tuberculous meningitis, nine, or 1.3 per cent., showed the bovine type of bacillus; among 132 patients between 5 and 16 years of age, thirty-three, or 25 per cent., showed the bovine type; among 120 patients under 5 years of age, fifty-nine, or 49 per cent., showed the bovine type. The striking feature of these figures is the alarming percentage of the bovine infection in children under 5 years. Undoubtedly this is due to the facts that milk, which is the probable

3. Griffith, A. S.: The Bacteriologic Characteristics of Tubercle Bacilli from Different Kinds of Human Tuberculosis, J. Path. & Bacteriol. **23**:129 (Feb.) 1920.

4. Novick, N.: Incidence of Bovine Infection in Tuberculous Meningitis, J. M. Research **41**:239 (Jan.) 1920.

CLINICAL DEPARTMENT

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Peripheral gangrene following diphtheria is of very rare occurrence. Ker [1] mentions the condition but states that he never saw a case. He refers to Rolleston,[2] who saw a case in 1910 and who was able to collect ten others from the literature at that time. Robbins [3] published a review of twenty-five cases of peripheral gangrene following diphtheria. The next important contribution to the subject was a critical and exhaustive résumé of the literature by Bailey.[4] No new case has been reported since. Our case is the fourth to be observed and reported in America, the previous ones having been published by Vedder (1879), Ward (1894) and Munn (1894).

REPORT OF CASE

History.—Abraham A., 6 years old, gave a history of having had a sore throat for four days without having received any medical attention. On the fourth day, a physician was called. He made a diagnosis of diphtheria and administered 15,000 units of antitoxin and advised removal to a hospital.

Examination.—The boy was admitted to the Kingston Avenue Hospital, April 26, 1920. He was poorly nourished and pale. Eyes and ears were negative. His throat showed an involvement of the fauces and pharynx, the membrane extending over both tonsils, uvula, posterior nares, nasopharynx and the pillars of the soft palate on the left side. Glandular involvement was moderate. The lungs were negative. The heart sounds were of good quality, rapid but no murmurs. The spleen was negative. The liver extended over to the left and could be felt about 2 inches below the free border of the ribs. He was given an additional 25,000 units of antitoxin intramuscularly.

Course.—Seven days after admission, the heart sounds became weaker in muscular tone and irregular. On the next day, he complained of severe pains in the left foot. There was a difference in the temperature between the two lower extremities, the left feeling colder to the touch. Purplish colored ecchy-

* Received for publication, Oct. 28, 1921.

* From the Kingston Avenue Hospital for Contagious Diseases, Department of Health.

1. Ker, C. B.: Infectious Diseases, Oxford University Press, London, Ed. 2, 1920.
2. Rolleston, J. O.: Brit. J. Child. Dis. **7**:529, 1910.
3. Robbins, F.: Juvenile Peripheral Gangrene in Infectious Diseases; Diphtheria, Med. Rec. **94**:620, 1918.
4. Bailey, L.: Occlusion of the Arteries of the Limbs in Diphtheria, Internat. Clin. **2**:157, 1920.

motic areas were irregularly distributed over the skin of the left thigh and leg. These disappeared by the following day but the toes of the left foot seemed to be of a blue color as compared with the pink color of the right foot. The thigh and leg had become somewhat warmer to the touch. Sensation was lost in the lower half of the left leg and foot, and there also was an apparent weakness of the same limb which caused it to hang flaccid. The reflexes were altered, in that the knee jerks were absent on both sides, the plantar reflex was absent on the left but present on the right; ankle clonus was negative on both sides, Oppenheim sign was normal on the right side but no response was elicited on the left; no Babinski or Kernig on either side. The pain in the left leg and foot was severe enough to necessitate the administration of morphin.

Coincidently with these local changes, the heart condition had become progressively worse so that on the twelfth day in the hospital there was a pronounced myocarditis with a gallop rhythm, reduplicated second sound and a tumultuous heart action. There were no murmurs. The throat was clear of any exudate but still gave a positive diphtheria culture. A posterior palatine paralysis with nasal regurgitation of fluids had developed. The child, however, was in an apparently comfortable condition.

Examination of the pulsation in Scarpa's triangle showed that it was present on both sides but not as pronounced on the left side as on the right. The popliteal pulsation was also not as definite on the left side as on the right.

The bluish discoloration of the left foot persisted, this being present on the dorsum and to a lesser extent on the plantar surface, being accompanied by a dilatation of the veins. The foot was swollen and waxy in appearance. The condition ameliorated with the establishment of a collateral circulation so that the foot became warmer to the touch and the color picture changed so that a few days later the dorsum presented two zones. From the ankle to the toes, the color was a deep cyanotic purple of uniform intensity, while just above and around this area was a zone of purplish red hyperemia. The deep purplish hue extended to the plantar surface. The cyanotic zones on both surfaces were swollen, edematous and hard to the touch.

Eight days subsequent to the involvement of the left foot, the boy experienced a sharp pain in the right foot. Within a day or two this was followed by a sensation of cold in the right foot and the appearance of irregularly distributed purplish areas on the dorsum. The foot became swollen. The toes became involved and then the heel. Within a few days, however, the cyanosis of the toes and dorsum of the foot gradually disappeared, but the discoloration on the heel remained, attaining the size of a silver trade dollar. The temperature on the right side gradually became lower than that on the left, especially from the knee down, the foot itself being almost ice cold. The cyanosis was not as pronounced as in the left foot, nor were the two color zones as definite. Within a week after the onset of the process in the right foot, the condition had improved to such an extent that the gangrene was limited to a small portion of the heel.

The process in the left foot became confined to the toes, a small portion of the plantar surface and 2 inches above the metatarsal phalangeal junction on the dorsum, the affected area being of a blackish purple color, hard in consistency and not painful. A sharp line of demarcation formed between this area and a surrounding one of a reddish pink. Within a month subsequent to the onset, the toes of the left foot showed a beginning desiccation, the dry gangrene also including a small portion of the plantar surface and some distance above the toes on the dorsal surface. The gangrene on the right heel was later confined to the skin and a slight area of superficial tissue.

Sloughing of the tissue ensued at the line of demarcation in both feet, resulting in a natural amputation of the gangrenous area in the right heel and a separation of the tissues down to the bone at the metatarsal phalangeal junction in the left foot. This process was permitted to continue for two months until the condition of the child had improved.

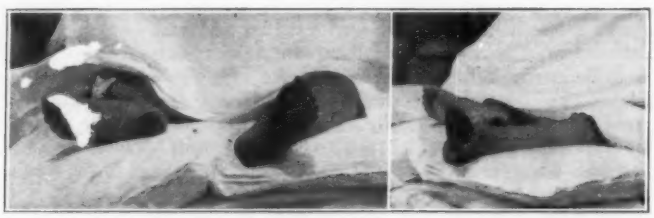
Operation.—August 30, about four months after the onset of the diphtheria, an operation was performed by Dr. Dangler, consisting of amputation through the metatarsal phalangeal joint of the left foot. By this time, the general condition and the cardiac lesion had both improved to such an extent that the gallop rhythm had disappeared and the myocardium assumed a stronger muscular quality.

The boy was discharged from the hospital within two weeks after the operation. At the present time, he is able to walk without any noticeable deformity.

Laboratory Findings.—Cultures: During his stay in the hospital throat cultures were positive for *B. diphtheriae* at the onset, while the nose cultures were always negative. At no time was any growth of diphtheria bacilli found in the blood. Three blood cultures were sterile. The Wassermann reaction was negative.

Blood: Red blood cells, 5,000,000; white blood cells, 16,600. Polymorphonuclears, 60 per cent.; lymphocytes, 39 per cent.; eosinophils, 1 per cent. Hemoglobin, 80 per cent. The coagulation time was four minutes.

The chemistry of the blood was studied by Dr. C. M. Anderson of the Long Island College Hospital: Urea nitrogen, 12 mg. per hundred c.c.; sugar, 76 mg. per hundred c.c.; urea, 25.68 mg. per hundred c.c.; uric acid, 3.1 mg. per hundred c.c.; creatinin, 1.6 mg. per hundred c.c.



Gangrene of heel of right foot and toes of left foot.

Urine: Urinalysis at the onset showed a trace of albumin with a specific gravity ranging from 1.010 to 1.030, always acid, sugar always absent, and occasionally pus cells, hyaline and granular casts. This all cleared up later.

Treatment.—This consisted of stimulation by means of whisky, camphor and epinephrin chlorid. Morphin was at times needed to control the pain. The lower extremities were encased in a hot air chamber which was arranged by fitting up a wire tent over which was placed the bed sheeting and a blanket to prevent the escape of the heat which was furnishes by an electric bulb within the chamber.

DISCUSSION

The delay in obtaining medical aid permitted the local spreading of the diphtheritic membrane and the accumulation of the diphtheria toxin in the system. While it is not known if the gangrene in these cases is the result of a massive diphtheritic intoxication or a superadded infection by some other organism, it seems plausible to feel that in this case the late administration of antitoxin permitted an intense diphtheritic toxicity. In spite of the severity of the disease, diphtheria bacilli were never found in the blood in the three examinations made. That the diphtheria bacillus is not very often found in the blood in

diphtheria was shown by Rodelius, who found this organism in only three cases out of 187 (196 withdrawals and tests).

Our case, like others in the literature, occurred in the hypertoxic type of diphtheria in which symptoms of cardiac insufficiency had already developed and after the local throat symptoms had disappeared. The course was the typical one of myocarditis—sluggish circulation, low blood pressure and insufficient collateral circulation. It is very difficult to state positively whether the condition was due to a local thrombus as the result of a local acute arteritis or to a migrating clot originating in the heart. Bailly and Robbins think that the condition is due to a migrating clot following the myocarditis. Those who are interested in the controversy as to whether peripheral gangrene following diphtheria is due to a thrombosis or an embolus are referred to Bailly's recent paper on the subject.[4]

Surgical intervention was postponed in our case because we felt that the child's general condition at the onset was too critical to subject him to any operative procedure. Later, when his condition had improved and the line of demarcation had made its appearance, it was thought best to permit a natural amputation in the hopes of saving a larger portion of his foot. The results amply justified our waiting.

PROGRESS IN PEDIATRICS

RÉSUMÉ OF LITERATURE (1920) ON TUBERCULOSIS IN CHILDREN *

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MODE OF INFECTION

J. W. ALLAN [1] is of the opinion that antenatal tuberculosis is more common than is generally believed and that many children are born with "seeds" of the disease lying latent which at a later period of life give rise to manifest tuberculosis. He thinks the placenta offers the most likely portal of entry for the tubercle bacillus, and quotes Bonny, who says that, despite the normal appearance of the fetal organ and of the placenta, tuberculosis has resulted from inoculation of animals with portions of these tissues and with blood from the placental circulation. Allan thinks that to account for the subseqent development of tuberculosis in the animals inoculated these apparently healthy tissues must have contained some "seed" or inverted form of the tubercle bacillus.

M. DUBOIS [2] adds the report of a case of intrauterine tuberculous infection to those already found in the literature. A woman suffering from miliary tuberculosis gave birth, prematurely, to a child. Forty-two days later she died and necropsy showed, besides the miliary tuberculosis, an old caseous tuberculosis of the left tube, of the endometrium, and a diffuse tuberculous peritonitis. The miliary tuberculosis originated either from a large tubercle in the right renal vein or from caseated tubercles found in the wall of the small uterine vessels.

The child, removed at once from the mother, developed poorly and died on the fifty-fourth day. The necropsy showed an old softened lesion in the right upper lobe with caseation of the right bronchial lymph glands, as well as a generalized miliary tuberculosis. The finding in the mother of a tuberculosis of the endometrium, which involved the site of the placenta and the age of the pulmonary and bronchial gland tubercles speak for an intrauterine infection either of hematogenous origin or due to aspiration of the amniotic fluid. The author

* Received for publication Dec. 10, 1921.

1. Allan, J. W.: Prenatal Tuberculosis, Glasgow M. J. **93**:1 (Jan.) 1920.

2. Dubois, M.: Intrauterine Tuberculous Infection, Schweiz. med. Wchnschr. **50**:772 (Aug. 26) 1920.

thinks the latter more probable because of the presence of the oldest lesions in the lung of the child and the findings in the uterus of the mother.

BACTERIOLOGY

A. STANLEY GRIFFITH [3] has tried to ascertain the relative proportion of the human and the bovine types of tubercle bacilli in different kinds of human tuberculosis. Of twelve cases of tuberculous meningitis, ten were caused by the tubercle bacillus of the human type and two by that of the bovine type. In one instance the cow's milk supplied to the patient was found to contain virulent tubercle bacilli, indentical in cultural characteristics with the strain from the meninges of the child.

Of seventeen cases of phthisis, sixteen were caused by the human bacillus and one by the form of bacillus recently found in various kinds of human tuberculosis and in one case of simian tuberculosis. Of twelve miscellaneous cases (three of bone and joint tuberculosis, eight of glandular tuberculosis, one of intermuscular abscess) nine were caused by the human type of bacillus, two by the bovine type, and one by a type which resembled the bovine but differed slightly in cultural characteristics and virulence.

From sixty cases of scrofuloderma, fifty-two cultures of the tubercle bacilli were obtained. Of these, sixteen showed the bovine type of bacillus, four a type less virulent than the ordinary bovine bacillus, and thirty-two the common human type.

The author reports that in England 1,068 cases of tuberculosis have been examined for the type of tubercle bacillus, 803 showed the human type, 194 the bovine, and five a mixed type.

N. NOVICK [4] has studied the incidence of bovine infection in tuberculous meningitis. He quotes Park and Krumwiede, who found 15 per cent. of bovine infection in tuberculous meningitis among 1,000 cases of all forms of tuberculosis, and Rosenau, who analyzed 1,040 cases of tuberculous meningitis, which included those of Park and Krumwiede. Rosenau's figures were as follows: Among 685 patients 16 years of age or over, with tuberculous meningitis, nine, or 1.3 per cent., showed the bovine type of bacillus; among 132 patients between 5 and 16 years of age, thirty-three, or 25 per cent., showed the bovine type; among 120 patients under 5 years of age, fifty-nine, or 49 per cent., showed the bovine type. The striking feature of these figures is the alarming percentage of the bovine infection in children under 5 years. Undoubtedly this is due to the facts that milk, which is the probable

3. Griffith, A. S.: The Bacteriologic Characteristics of Tubercle Bacilli from Different Kinds of Human Tuberculosis, J. Path. & Bacteriol. **23**:129 (Feb.) 1920.

4. Novick, N.: Incidence of Bovine Infection in Tuberculous Meningitis, J. M. Research **41**:239 (Jan.) 1920.

means of transmitting the tubercle bacillus, is the chief element in the diet of children and that the bovine bacillus is much more virulent in children.

The author's series consisted of forty-eight cases of tuberculous meningitis; two were in adults and forty-six were in children of from 4 months to 16 years. Forty-eight strains of tubercle bacilli were isolated from the cerebrospinal fluid in these cases and only three proved to be of the bovine type. One of the bovine strains was isolated from a case of meningitis in a baby 22 months old, one in a 6 year old child and one in a 16 year old patient.

SYMPTOMATOLOGY

J. V. Cooke and T. C. Hemplemann [5] believe that many children are infected with the tubercle bacillus and for a variable length of time harbor somewhere in their bodies a pathologically active tuberculous focus, which may be unsuspected. To this form is applied the term masked juvenile tuberculosis. The authors think that masked juvenile tuberculosis presents a sufficiently distinct clinical type to deserve a prominent place in the category of tuberculous affections in childhood. The clinical picture may be sketched as follows: A history of frequent coughs and colds with or without known exposure to tuberculosis; attacks of unexplained fever, often with afternoon elevations; anorexia; loss of weight, and asthenia. On examination there is found malnutrition, occasionally anemia, and signs in the chest referable to enlarged tracheobronchial nodes. In some instances there may be phlyctenular disease or skin tuberculids. The Pirquet or intracutaneous tuberculin test is positive and three-fourths of the children over 4 years of age give a positive complement fixation test for tuberculosis. The chest findings may be verified by the roentgen ray, which not infrequently reveals also unsuspected lesions of varying size and age in the lung parenchyma. The diagnosis must rest on a review of all findings, but the authors emphasize the value of the complement fixation test in calling attention to this class of cases. As to the fate of children with marked tuberculosis, three possibilities suggest themselves. By far the commonest is regression of the lesion with recovery, and the authors are of the opinion that these relatively harmless lesions may stimulate the body to produce certain protective substances against future infections. A second outcome is the development of a more manifest tuberculosis through extension of the process. And the third is the persistence of the marked lesions to adult life with a possible later development of active tuberculosis.

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5. Cooke, J. V., and Hemplemann, T. C.: Masked Juvenile Tuberculosis, Am. Rev. Tuberc. **4**:660 (Nov.) 1920.

Cooke and Hemplemann believe that the recognition of this marked form of tuberculosis is a matter of the greatest importance, because the inauguration of an antituberculosis regime results usually in a reasonably good chance of recovery.

P. Armand de Lille [6] describes the evolution of tuberculosis in older children. If the infection is not a massive one, the onset is very insiduous and the disease becomes manifest only after an infectious disease or an indoor winter life, which lowers the resistance and suppresses the formation of antibodies. There then develop fatigue, stationary weight or loss of weight, listlessness, anorexia, and usually an evening rise in temperature. The child, however, does not appear to be ill. After several weeks these symptoms disappear, but the Pirquet test, previously negative, is found to be positive. At this stage physical and roentgen-ray examination reveal enlarged glands in the tracheobronchial region. If the child's resistance is sufficient, the disease then remains latent until adult life, when the glands gradually diminish in size and sclerose. If, however, the resistance is not great enough to overcome the infection, the second stage of generalization, namely, a miliary tuberculosis, results. The clinical symptoms then depend on the degree of generalization. If widespread, there is high temperature, rapid pulse, emaciation, lassitude, without signs of localization, which last from ten to twenty days, when signs of pulmonary or meningeal involvement appear. If the tubercules are very discrete there may be prolonged fever without localized signs, the "typho-bacillose" of Landouzy; there may be only a single localization, as a pleuritis, peritonitis or joint effusion. Sometimes only a few tubercles are scattered in various organs, where they become sclerosed or resorbed or develop into local tuberculous foci.

Nobecourt and Paraf [7] believe that chronic pulmonary tuberculosis in children may have an acute rapid onset or a slow progressive one. In cases with an acute onset there are general symptoms, as fever, emaciation, weakness, anorexia; functional signs, as slight dyspnea, a dry cough, or a paroxysmal cough, like whooping cough. The physical signs depend on whether the lesion is a tracheobronchial adenopathy or a dry pleurisy located at the apex, in the fissures, or at the hilus.

Cases with a slow progressive course occur usually at puberty. The symptoms are those of an active tuberculosis, emaciation, fatigue, pallor, anorexia, digestive disturbances, tachycardia and arterial hypo-

6. Armand-de Lille, P.: Tuberculosis in Older Children, Bull. méd. Par. **34**:999 (Nov. 13) 1920.

7. Nobecourt and Paraf: Chronic Pulmonary Tuberculosis in Older Children, Rev. de la Tuberc. **1**:329, 1920.

tension. The physical signs are difficult to detect and to interpret. A normal resonance at the apex may be accompanied by a feeble or rough low pitched respiration. Feeble respirations are not characteristic and may be due to imperfect nasal breathing, tracheobronchial adenopathy, an old pleurisy, cardiac disease or an asymmetrical thorax. The first valuable signs at the apex are impaired resonance, increased resistance, prolonged expiration and exaggerated voice sounds. A prolonged blowing expiration is corroborative evidence. Enlarged tracheobronchial glands, however, can cause an atelectasis and congestion of the apex and can simulate a tuberculous process. The roentgen ray is an important aid in differentiation.

H. Eliasberg and W. Neuland [8] have studied a condition found occasionally in the lungs of tuberculous children, which they term "epituberculous infiltration." Clinically, children with this condition are pale and emaciated; they cough, have no appetite, and frequently have a slight temperature. These symptoms come on gradually. Physical examination reveals a massive dulness of an entire lobe, usually one of the upper lobes, with bronchial breathing but no râles—findings out of all proportion to the slight general disturbance. The sputum does not contain tubercle bacilli; but all these patients show a positive Pirquet reaction. Often there are other evidences of tuberculosis, as fistulae, tuberculous glands or tuberculids. There is usually a family history of tuberculosis. The disease runs a benign course; the symptoms disappear and the infiltration is gradually absorbed, until in the course of months it has disappeared entirely. No evidences of contraction of the lung, as drawing in of the thorax, displacement of the heart or mediastinum, or bronchiectasis, accompany resolution.

The authors believe the condition to be a chronic, nonspecific infiltration, with a simultaneous tuberculous infection and that it must be differentiated from the gelatinous infiltration of Laennec, the chronic bronchopneumonias, which follow whooping cough and influenza, especially when accompanied with a pleural exudate, foreign bodies, stasis, open ductus botalli, and, in young children, a persistent thymus.

As the infiltration ultimately subsides, no treatment is necessary beyond measures to promote resolution and aborption.

A. Wolff-Eisner [9] believes that in tuberculous individuals exudative manifestations appear frequently and that there is a hypersensi-

8. Eliasberg, H. and Neuland, W.: Epituberculous Infiltration of the Lung in Children, Jahrb. f. Kinderh. **93**:88, 1920.

9. Wolff-Eisner, A.: The Relation between Tuberculous Infection and Constitutional Diathesis, München med. Wchnschr. **67**:93 (Jan. 23) 1920.

tiveness not only to the specific proteid of the tubercle bacillus but also to other proteids (nuclein, albumoses, etc.). In tuberculous children variations in the normal electrical reactions also occur freqently. He thinks manifestations of exudative diathasis and spasmophilia are due not only to nutritional disturbances and absorption of toxins from the intestine but also to the absorption of foreign proteids from any source, hence they are evidences of hypersensitiveness or anaphylaxis.

A. WOLFF-EISNER [10] has made a further study of the nervous excitability in tuberculous children. He thinks that if there is any relation between tuberculosis and the exudative and spasmophilic diathesis the electrical reactions in these conditions should be analogous. The electrical reactions of fifty-two children suffering from osseous tuberculosis were taken. As they were all between 6 and 14 years of age, there were no signs of spasmophilia. The results were interesting. The electrical reactions varied from the normal but were not characteristic of those of the exudative and spasmophilic diatheses, in that the A.C.C. was greater or equal to the C.C.C. Nevertheless, Wolff-Eisner believes these results shows a relation between tuberculosis and the diatheses of childhood.

C. MUNIGURRIA [11] reports a case of cardiotuberculous cirrhosis in a 6 year old boy. When seen by him, the child had been ill one year with pain in the extremities, fever, general weakness, insomnia, and loss of appetite. On examination there was dulness over the right apex, with bronchial breathing, pain over the sterum and arhythmia. While under observation, the child developed a general edema, icterus, cyanosis of the extremities and dyspnea, with dulness and râles over the right base. The heart dulness was increased. The liver was enlarged and painful; the spleen was palpable. Death occurred six months after the first examination. Necropsy showed biliary ascites, tuberculosis of the mesentery glands, fatty degeneration of the liver, miliary tuberculosis of the lungs, tuberculous pericarditis with the pericardium adherent to the pleura and diaphragm. A large tubercle was found at the opening of the right ventricle.

R. SIMONINI [12] reports an instance of tubercle of the myocardium in an 18 month old infant. The tumor was the size of a nut, located on the outer side of the right auricle. It penetrated into the myocardium but not into the auricle.

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10. Wolff-Eisner, A.: Changes in the Electrical Excitability in Tuberculosis of Childhood, Beitr. z. Klin. d. Tuberk. **45**:283 (Nov. 25) 1920.

11. Munigurria, C.: Cardio-Tuberculous Cirrhosis, Abstr. Zentralbl. f. d. ges. Kinderh. **9**:577 (Nov.) 1920.

12. Simonini, R.: A Report of a Large Tubercle of the Heart in an Eighteen Month Old Infant, Abstr. Jahrb. f. Kinderh. **94**:67, 1921.

T. H. and H. O. GUNEWARDENE [13] report a case of extensive primary tuberculosis of the heart in a 6 year old boy. The child died ten days after admission to the hospital. At necropsy both ventricles were hypertrophied and dilated. In the right ventricle, just above the attachment of the tricuspid valves, were two nodular masses about 1 c.mm. in diameter. Small isolated areas of firm, white tissue infiltrated the interauricular septum and the wall of the right auricle and the heart muscle at the root of the pulmonary vein. The visceral pericardium was completely adherent, but no tubercles could be seen. On section there was an inurated ulcer 1 cm. × 1½ cm. in diameter. bacilli. Tuberculous lesions were not found by the naked eye in any of the other organs. The authors regard this as a case of primary tuberculosis of the myocardium. They found forty-one cases of tuberculosis of the myocardium reported in the literature but only one with a similar location and no other in which the disease was primary in the myocardium.

Under the name of hyperplastic tuberculosis of the small intestine J. RANSOHOFF [14] describes a tuberculous process, which because of its chronicity permits of excessive effort at repair and assumes the guise of a neoplasm. In most cases the disease involves the cecum and terminal coils of the ileum, and is the primary localization of the tuberculosis.

The author's patient was a 9 year old girl, who had previously been operated on for tuberculous glands. For two or three years the patient had complained of colicy pains, which occurred four or five times a day, soon after taking food but which had no relation to bowel movements. The pain was localized in a small area, immediately to the left and slightly below the umbilicus. Examination of the abdomen showed a mass about the size of an apple in this location. At operation a growth was found at the lower end of the jejunum, which involved about seven inches of the intestine. The lymph glands of the mesentery were enlarged. About ten inches of the intestine was resected and recovery was uneventful.

The tumor mass was found to consist entirely of the intestinal wall. On section there was an indurated ulcer 1 cm. × 1½ cm. in diameter. Microscopically, the tumor consisted of small round cells and polymorphonuclear cells; rarely a multinucleated giant cell occurred. In spite of the resemblance to a sarcoma, the author believes the growth to be tuberculous because of the history and the presence of the ulcer.

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13. Gunewardene, T. H. and Gunewardene, H. A.: Extensive Primary Tuberculous Disease of the Heart, Proc. Roy. Soc. Med. Lond. Sec. Dis. Child. **13**:38 (March) 1920.

14. Ransohoff, J.: Hyperplastic Tuberculosis of the Small Intestine, Ann. Surg. **72**:196 (Aug.) 1920.

He considered, however, the possibility of a sarcomatous growth in primary tuberculous tissue.

J. H. M. KNOX [15] reports a case of tuberculoma of the midbrain associated with tuberculous meningitis. The patient was a colored boy 3 years of age, who was taken to the hospital because of general weakness, trembling and drooping of the eyelids. The patient had appeared to be perfectly normal until six months before, when he stopped crying almost completely. Four months later it was noted that his hands shook when he fed himself. About the same time his eyes began to droop. On examination his general condition seemed excellent. The eyes showed the following: The pupils reacted to light, the left better than the right. There was a marked bilateral ptosis of the eyelids and a definite lateral deviation of the eyeballs to the right, also an occasional lateral nystagmus of the right eye. The child was sent home but returned for admission two weeks later, when a distinct paraplegia of both lower extremities was noted. The spinal fluid, obtained under a marked increase in pressure, gave a reaction for globulin, and contained an increased number of cells of the mononuclear type. The roentgen-ray examination of the head showed a moderate internal hydrocephalus and a probable tumor above the sella turcica. The Pirquet test was frankly positive. Ten days after admission a slight rigidity of the neck was noticed and from this time on the child grew constantly weaker. Drowsiness gradually deepened, general convulsions developed, and the boy died forty-two days after the first observation.

The acquired ptosis, the tremor of long standing, and the gradually developing external strabismus led Knox to venture the diagnosis of tumor of the midbrain interfering with the nuclei of the third and fourth cranial nerves. The positive Pirquet reaction and development of a meningitis toward the end suggested that the tumor was of tuberculous nature. This diagnosis was confirmed at necropsy when a solitary tubercle of midbrain and of the right parietal lobe, and a tuberculous meningitis were found.

H. KOCH [16] is of the opinion that occasionally recovery takes place in cases of brain tubercle. He draws this conclusion from the study of three cases and from the review of the literature on the subject. His first case was a 5 year old girl who entered the hospital because of vomiting, ataxic gait and a positive Romberg's sign. While under observation there developed a marked tremor. The Pirquet reaction

15. Knox, J. H. M.: Lesions in the Midbrain, Am. J. Dis. Child. **20**:436 (Nov.) 1920.

16. Koch, H.: Contribution to the Etiology of Brain Tubercle, Ztschr. f. Kinderh. **24**:197 (Dec.) 1919.

was positive. The child remained in the hospital four months; on discharge all symptoms had disappeared, except the positive Romberg. The second case was that of a 9 year old child, who had for eight weeks attacks of dizziness and vomiting. Fourteen days before entering the hospital she became unconscious and developed a left sided paralysis. On entrance there was ataxic gait, a positive Romberg's sign, a paralysis of the left abducens nerve, and hyperesthesia of the left cornea. After seven months' observation the gait became normal and the child was discharged with no evidence of her illness, except the paralysis of the abducens nerve.

The third case was a 5 year old child, who was admitted to the hospital because of convulsions and muscular twitchings. The child was under observation for eleven months and the diagnosis of brain tubercle was based on the presence of irritative symptoms and a positive tuberculin test. At first the child showed no improvement and during an attack of measles had as many as twenty-three convulsions a day. Two weeks after the onset of the measles the convulsions subsided but recurred with greater severity about the fourth week. This period lasted fourteen days, when the convulsions ceased altogether. The author thinks that during the attack of measles there was a formation of miliary tubercles around the tuberculoma (he has seen this at necropsies) which caused the exacerbation of the convulsions. Their cessation was due to relief of pressure on nerves or blood vessels by absorption of inflammatory products or to the opening of the cerebrospinal canal, which could have been obstructed by the inflammatory products.

Koch discusses the possibility of permanent cure and cites a few instances reported in the literature. Nevertheless, he believes the prognosis is usually unfavorable, chiefly because the tubercle is a metastatic tuberculous process and the prognosis depends upon the extent of the original disease and because, too, there is a tendency for patients with brain tubercles to develop tuberculous meningitis.

A. WAGNER[17] reports a case of solitary tubercle of the spinal medulla in a 14 year old boy. For three weeks before entering the hospital he had complained of severe pain in the lumbar region and right leg, vomiting and headache. Examination on entrance showed marked pallor and emaciation, with tuberculous lesions on the lower extremities. There was tenderness over the spine and edema in the lumbar region. The Pirquet test was positive. The muscles of the right leg, especially those of the thigh and buttocks, were atrophic and paralyzed. There was a positive Babinski and Kernig's sign. Lumbar

17. Wagner, A.: Contribution to the Diagnosis of Solitary Tubercle of the Spinal Cord, Ztschr. f. Kinderh. **25**:322 (June) 1920.

puncture gave a slightly turbid fluid under pressure, with a positive Nonne and 240 cells to the cubic centimeter, only 8 per cent. of which were neutrophils, the remainder being polymorphnuclear cells. The clinical diagnosis was solitary tubercle of the brain; tuberculous meningitis; tuberculosis of the skin. The cause of the paralysis of the leg was undecided. The child died and necropsy showed old caseous tuberculosis of the bronchial glands, pulmonary tuberculosis, miliary tubercles of spleen, liver, and kidneys, multiple conglomerate tubercles in the brain, chronic internal hydrocephalus, and tuberculous ulcers in the colon. In the lumbar region of the cord was a cherry sized tubercle, which accounted for the paralysis of the right leg.

According to the writer, solitary tubercles of the spinal cord are rare. The disease usually begins with weakness, pain and paresthesias in the extremities; later there is a disturbance in temperature sense. Muscular atrophy and paralysis occur early. Compression myelitis and spinal syphilis are to be considered in differential diagnosis. Remissions and exacerbations of symtoms and the roentgen-ray finding of spinal caries speak for compression myelitis and a positive Wassermann reaction for syphilis.

SCHMINCKE[18] reports a case of solitary tubercle in the cervical cord. The patient was an 8 month old child who for three months had lost weight and had cried continuously. The child did not attempt to sit up or to use the right arm. There was also less power in the right than in the left leg. While under observation, the child became apathetic and developed stiffness of the neck and general convulsions.

At necropsy there was found a disseminated caseous tuberculosis of the left upper lobe, caseous tuberculosis of the bifurcation and hilus glands, miliary tuberculosis of the liver, spleen and kidneys, tuberculous basilar meningitis. In the region of the cervical enlargement of the spinal cord the dura was adherent to the pia. The cervical enlargement was greater than normal, and on cross section there was found a caseous area, the size of a pea.

A. GENDRON[19] reports three cases of erythema nodosum and one of a miliary eruption in children of a tuberculous family. The disease had a period of incubation of four days, in all of them, a period of invasion with the usual phenomena of infection, and a period of eruption of twelve days, followed by complete cure. Four months later one of the children developed a pleurisy. In one the roentgen ray showed an opaque zone near the fissure in the left lung and the other two children gave positive tuberculin reactions. These facts cause

18. Schmincke: A Case of Solitary Tubercle in the Cervical Cord, Jahrb. f. Kinderh. **92**:407, 1920.

19. Gendron, A.: Erythema Nodosum and Tuberculosis, Bull. et mém. Soc. méd. d. hôp. de Par. **44**:475 (March 26) 1920.

the writer to believe that the four children were already affected with tuberculosis, when they became ill with the erythema. He is of the opinion that tuberculosis creates a favorable ground for the development of erythema nodosum.

L. LAEDERICH and C. RICHET [20] discuss the relation of erythema nodosum to tuberculosis. They believe clinical, biologic and bacteriologic studies point to a close connection between the two conditions. As regards clinical facts, erythema nodosum has often been observed in patients with open tuberculosis. It has appeared in persons apparently well but who soon after the attack develop signs of an acute tuberculosis; and it has appeared simultaneously with other manifestations of acute or subacute tuberculosis.

Biologic studies are very suggestive. Patients with erythema nodosum almost invariably give a positive tuberculin test. Injection of these patients with tuberculin causes the appearance of a nodule of erythema nodosum. Also often in tuberculous patients an intradermal injection of tuberculin will cause the appearance of the large red nodules of erythema nodosum.

In experimental animals the bacillus of Koch has been found in the blood during an attack of erythema nodosum and a number of observers have reported finding this organism in the lesions. Although the writers do not think that all cases of erythema nodosum are of tuberculous origin, they conclude from the facts they observed that tuberculosis is an important factor in the etiology.

E. WARD [21] is of the opinion that erythema nodosum is a toxic manifestation of many different conditions, one of which is tuberculosis. That the occurrence of erythema nodosum and tuberculosis is not merely a coincidence is proved by the fact that erythema nodosum has been known to occur after an injection of tuberculin. The author has noticed the appearance of erythema in tuberculous patients, when a chronic condition becomes more acute and when the symptoms of tuberculosis first become noticeable in a patient under observation as a contact.

T. MCCRIRICK [22] reports a case of tuberculosis verrucosa cutis of the foot in a 12 year old boy. The lesions were of four years standing and consisted of a warty growth, which involved the greater part of the thin skin of the sole and inner side of the foot. The height of the growth above the general skin level was three millimeters. The

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20. Laederich, L. and Richet, C.: Erythema Nodosum and Tuberculosis, Rev. de la Tuberc. **1**:229, 1920.

21. Ward, E.: Erythema Nodosum and Tuberculosis, Brit. M. J. **2**:811 (Dec. 20) 1919.

22. McCririck, T.: Tuberculosis Verrucosa Cutis of the Foot, Brit. J. Child. Dis. **17**:26 (Jan.-March) 1920.

source of infection was evidently a sister, who had at the time of appearance of the lesions multiple tuberculous abscesses. The child ran about barefoot in warm weather and a cut or scratch evidently became inoculated from carelessly handled dressings.

C. WITH [23] observed an atypical tuberculous eruption, which appeared on the extremities of a 7 year old child, being treated for lupus. On the extensor surface of the upper and lower extremities was a bright red eruption, consisting of lentil sized papules, slightly infiltrated and with central scaling. There was a diffuse scaly infiltration of the skin surrounding the lesions.

D. GUTHRIE [24] found thirteen cases of tuberculous origin among seventy-nine cases of chronic otitis media, in which the cause had been noted. All cases, except one, occurred in infants 1 year of age. The disease was characterized by a painless, insidious onset. The discharge was frequently the first sign of the disease. Facial paralysis was noted in seven cases and enlarged parotid glands in all. The author believes that these cases are due to milk infection and that the infection is carried to the middle ear by way of the eustachian tube.

B. S. VEEDER and T. C. HEMPELMANN [25] subjected 196 children with phlyctenular disease to a careful study to determine the possible presence or absence of tuberculous infection. The study revealed an intimate association of the two diseases. Skin tuberculin tests were positive in more than 92 per cent. of the cases. The results of the complement fixation test for tuberculosis were strikingly similar to those obtained in cases of proved tuberculosis. Tuberculous lesions involving other organs than the eye were definitely demonstrable in more than half the cases. Cough, malnutrition and history of exposure to other cases of tuberculosis were frequent.

TUBERCULOSIS OF THE TRACHEOBRONCHIAL AND MESENTERIC LYMPH NODES

M. NOBECOURT [26] recounts the symptoms of tracheobronchial adenopathy. Respiratory disturbances are in proportion to the size of the glands. Dyspnea and shortness of breath are frequent. The dyspnea is more marked on exertion and in severe cases accompanied with expiratory difficulty in children under 3 years of age, and inspira-

23. With, C.: Atypical Tuberculid on the Arm of a Seven Year Old Child, Abstr. Zentralbl. f. d. ges. Kinderh. **10**:221 (Feb. 8) 1921.

24. Guthrie, D.: Thirteen Cases of Aural Tuberculosis in Infants, J. Laryngol. Rhinol. & Otol. **35**:99 (April) 1920.

25. Veeder, B. S. and Hemplemann, T. C.: Phlyctenular Ophthalmia and its Relation to Tuberculosis, Arch. Pediat. **37**:396 (July) 1920.

26. Nobecourt, M.: Tracheobronchial Adenopathy, Progrès méd. **35**:216 (May 15) 1920.

tory in children above 3 years. Two types of dyspnea are associated with enlarged bronchial glands, asthmatic attacks which come on suddenly, sometimes during the night, sometimes during the day, with difficulty in inspiration but quiet blowing expiration and spasm of the glottis which is accompanied by a rough noisy respiration. Aphonia and dysphonia due to paralysis of the recurrent laryngeal nerve may also occur—as may palpitation and difficulty in swallowing.

Enlarged tracheobronchial glands give rise to characteristic physical signs; dilated veins on the chest, but the glands must be very voluminous to cause this phenomenon; feeble expansion on one side of the chest; dulness and bronchial breathing in the intercostal and vertebral zones and D'Espine's sign. Evidences of passive congestion, such as diminished resonance and râles, are frequently found at the right base. In some children enlarged bronchial glands are accompanied by attacks of bronchitis, in others by a very obstinate bronchitis or bronchopneumonia. In these instances signs of pulmonary tuberculosis are found associated with those of tracheobronchial adenopathy. Radioscopy gives precise information of the pulmonary conditions.

Nobecourt calls attention to the fact that enlarged bronchial glands are not always due to tuberculosis. They may occur in the course of a bronchopneumonia, bronchitis or whooping cough. They are frequently associated with adenoid vegetations and are found in cases of hereditary syphilis and leukemia.

V. OHLEN,[27] discussing the early diagnosis of hilus gland tuberculosis, bases his conclusion on the study of seventy-seven children. He lays special stress on a failure to develop physically, the tuberculin reaction, and the roentgenogram. He thinks the most important of these is the failure to make satisfactory gain in development, associated with which is a condition of poor nutrition and a marked pallor of the skin and mucous membranes. Night sweats and general weakness and cough are concomitant symptoms. The cough is usually the symptom which causes the parent to consult a physician

V. Ohlen frequently used the Ponndorf tuberculin test, instead of the Pirquet. Four or five vaccination scratches, from 5 to 6 cm. long, are made near one another on the upper arm. These are intersected by three or four cross lines, so as to make a lattice work. Two drops of pure tuberculin are well rubbed into the scarification. Observations are made after forty-eight hours. By this method a larger amount of antigen comes in contact with the scarified area than with the Pirquet test.

The author thinks that in only occasional cases can a positive diagnosis be made by the roentgen ray alone and this is when sharply

27. v. Ohlen: Early Diagnosis of Hilus Gland Tuberculosis, Beitr. z. Klin. d. Tuberk. **45**:343 (Nov. 25) 1920.

defined hilus shadows are present. Repeated plates must be made at intervals, in order to draw correct conclusions. It is a valuable experience to see, on the one hand, how in the course of months hilus shadows become thicker, narrow streaks stretch out into the lungs, and new isolated shadows appear; or, on the other hand, to see how the hilus shadow becomes smaller, the cardiac outline clearer and the cardiodiaphragmatic angle becomes again visible. In all except one of the author's cases, in which the tuberculin test was positive, were there positive roentgenologic changes in the hilus region. Moreover, the intensity of the reaction was parallel with the severity of these changes.

K. KLARE[28] believes that D'Espine's sign is most valuable to establish the diagnosis of bronchial gland tuberculosis in children. Again and again he has proved its worth under control of the roentgen ray.

H. MERY[29] believes that the early diagnosis of tuberculous bronchial glands is the most important factor in the battle against tuberculosis in childhood.

A family history of tuberculosis and a previous history in the child of pleurisy, cervical adenitis, frequent attacks of bronchitis, a slow recovery from whooping cough or measles are important presumptive evidence of tuberculous bronchial glands. In examining the child attention is first called to emaciation, pallor, development of hairy growth, presence of cervical, axillary, and inguinal glands. Of the functional symptoms the paroxysmal cough, like whooping-cough, is the most important. Examination of the chest shows enlarged veins. Percussion of the anterior portion of the chest is more important than of the posterior. Here there is dulness and a resistance which extends two fingers' breadth to the right and left of the sternum. Dulness in the paravertebral area is important, as are modifications of respiratory and increased transmission of voice sounds. The author thinks a feeble respiratory murmur in this region is of important diagnostic significance. Rough breathing is frequently found over the bases, and crepitant râles due to transient pulmonary congestion. The roentgen ray should be used to complete the examination.

H. MERY and L. GIRARD[30] describe active forms of hilus tuberculosis in children. The active process may be confined to the glands or may involve the periglandular structure. If confined to the glands, there are more physical findings anteriorly than posteriorly. There is

28. Klare, K.: Spinal Ausculation in the Diagnosis of Enlarged Bronchial Glands, Ztschr. f. Kinderh. **27**:169 (Dec. 16) 1920.

29. Mery, H.: Early Diagnosis of Bronchial Gland Tuberculosis, Presse méd. **28**:873 (Dec. 4) 1920.

30. Mery, H., and Girard, L.: Active Forms of Hilus Gland Tuberculosis in Childhood, Rev. d. la Tuberc. **1**:289, 1920.

parasternal dulness in the two first intercostal spaces and a rough respiratory murmur. The dulness may be so marked that an apical or interlobar pleurisy or a hydatid cyst is suspected. The roentgen ray shows that the apices are clear, but there is present a paracardiac triangular shadow, with the base toward the heart.

If there is periglandular involvement besides the signs described, subcrepitant râles are heard posteriorly in the paravertebral spaces. General symptoms, such as fever, emaciation, loss of appetite, are also present. An interlobular pleuritis usually occurs and is manifested by severe pain. On the roentgenogram the interlobular pleuritis gives a transverse shadow which extends from the hilus to the axilla, with the base toward the heart and the apex toward the axilla.

W. PFEIFFER [31] adds a contribution to the value of direct tracheobronchoscopy in stenosis of the respiratory system from tuberculous bronchial glands. He believes that this procedure is not only of value in confirming the diagnosis of enlarged bronchial glands but has also a therapeutic worth. Broken-down bronchial glands can rupture into the air passages and cause suffocative attacks or death from suffocation. Before rupture of the gland the bronchoscope shows in nearly every instance a bulging, redness and swelling of the mucous membrane, which has a smooth satin-like appearance. Widening and flattening of the carina of the trachea is usually a sign of enlargement of the inferior tracheobronchial glands. The right side of the trachea and the right bronchus are more often affected than the left. In case of rupture the point of perforation can usually be demonstrated and cheesy or purulent masses are found in the air passages. The cheesy masses look yellowish-white or chalky and frequently have a very foul odor. They can be removed by suction, with absorbent cotton pledgets or foreign body forceps. Sometimes they are coughed up through the bronchoscope during the operation. Sometimes the pressure of the tube in the neighborhood of the perforation causes cheesy masses to be evacuated into the air passages. Granulation tissue frequently forms on the edges of the perforation after the gland has ruptured. Rupture usually takes place slowly. Portions of the gland, passing through the small opening, cause cough and suffocative attacks, like those caused by small foreign bodies which do not entirely obstruct the air passages. The cough is paroxysmal and accompanied by a spasm of the larynx. This is followed by a latent stage in which there are no symptoms. Gradually, however, usually in consequence of a severe coughing attack, the perforation becomes larger and the broken-down gland is protruded into the air passages, producing all degrees of

31. Pfeiffer, W.: Value of Direct Tracheobronchoscopy in Stenosis of the Respiratory System from Tuberculous Bronchial Glands, Beitr. z. Klin. d. Tuberk. **41**:197, 1919.

dyspnea—even to complete suffocation. Rupture of the gland into the air passages sometimes causes a subcutaneous emphysema, which spreads rapidly over the neck and thorax.

As to the treatment of tuberculous bronchial glands, if there are no symptoms of pressure, hygienic measures can be resorted to and many patients are cured permanently. If, however, there are symptoms of pressure, the patient should be taken to a hospital, where he can be under observation and examined with the bronchoscope. In children under 5, because of danger of subglottic swelling from pressure of the tube, a tracheotomy should first be performed. Tracheotomy alone is insufficient to prevent death from suffocation, in case the gland has already ruptured, though occasionally the obstructing gland is coughed up through the tracheotomy wound. By means of the bronchoscope the point of obstruction is located, the mucous membrane over the protruding gland opened, and the caseated masses removed. The operation must be preformed repeatedly because of the gradual breaking down of the gland.

As asserted by H. M. CHUTE,[32] mesenteric lymph nodes react to infection in a manner similar to lymph nodes in other situations. In children and adults enlarged mesenteric glands are one of the causes of abdominal pain, which gives no hint as to its origin until exploratory laparotomy is performed. In children the early history of the condition is characterized by vagueness. The child is anaemic and listless and suffers from loss of weight and appetite. Digestive disturbances, like diarrhea or constipation, are common. As the inflammatory process progresses, there occur attacks of abdominal pain, which shift about, probably because of the ease with which the nodes move within the mesentery. Fever and vomiting and moderate rigidity over the muscles may occur. If, as is frequently the case, the ileocecal glands are involved, the picture may be one of acute appendicitis. As the disease advances to abscess formation, the symptoms are more definite and localized. A tender mass is found in the abdomen with moderate muscle spasm. If rupture takes place, there are symptoms of generalized peritonitis. Mesenteric glands of long standing may become calcified, when a roentgen-ray examination may lead to an incorrect diagnosis of renal or ureteral stone. Enlarged mesenteric glands may cause intestinal obstruction from adhesion of the gut or omentum to a gland.

Chute emphasizes that in children recurrent attacks of abdominal pain with fever, little or no vomiting, constipation and loss of weight, should remind one of the possibility of tuberculous mesenteric glands.

32. Chute, H. M.: Enlarged Mesenteric Glands, Boston M. & S. J. **183**:409 (Sept. 30) 1920.

The diagnosis can sometimes be confirmed by combined rectal and abdominal palpation.

Treatment is surgical, followed by hygienic measures, and the prognosis is good.

E. GEHRELS [33] classifies as mesenteric tuberculosis only those cases in which the mesenteric glands alone are affected and omits all in which there are also intestinal or peritoneal lesions. He believes the tubercle bacillus can pass through the intestinal wall without causing specific changes. The bovine is the more common type of organism found. The disease is not frequent and in the author's experience was found in only 1 per cent. of 15,000 autopsies. Two thirds of the cases occurred in children. The writer discusses two forms, the acute and chronic. The acute form may be easily mistaken for other acute abdominal disturbances. In the chronic form there are recurring attacks of abdominal pain, usually located in the ileo-caecal region and associated with loss of weight and fever. Functional disturbances, like spastic constipation or diarrhoea, may occur. Intestinal obstruction and peritonitis are the most important complications. The diagnosis is difficult. The palpation of enlarged glands, the temperature curve, and the roentgen ray are aids. The lack of abdominal distention and sensitiveness to pressure help to differentiate the disease from appendicitis, which it resembles in the earlier manifestations. Tuberculosis of the mesenteric glands is more amenable to treatment than any other form of tuberculosis. Forced feeding, change of climate, artificial heliotherapy, deep abdominal roentgenotherapy, and tuberculin injections are all valuable procedures. Surgical intervention is indicated only when long continued internal treatment has failed.

DIAGNOSIS

P. GROSSER [34] emphasizes the following points in the diagnosis of early tuberculosis in children. Very important is an exact history of possible exposure to the disease. The temperature curve needs careful study. Irregular, often intermittent temperatures which last over a long period of time are suspicious. It must not be forgotten, however, that similar temperature curves occur in children with infections of the upper respiratory tract and in nervous children. Night sweats are not frequent in early tuberculosis. The involvement of three groups of glands is suggestive, namely: those at the angle of the jaw, those just above the clavicle, and the thoracic glands. Early involvement of the tracheobronchial glands is difficult to detect and the glands must

33. Gehrels, E.: Tuberculosis of the Mesenteric Glands, Deutsch. med. Wchnschr. **45**:44 (Oct. 9) 1919.

34. Grosser, P.: Diagnosis of Tuberculosis in Children, Deutsch. med. Wchnschr. **46**:369 (April 8) 1920.

be of considerable size before they cause symptoms of stasis or pressure or before signs can be obtained by percussion. Enlarged veins on the chest frequently occur in normal children and are of no diagnostic value. Pressure on the sympathetic nerve gives rise to inequality of the pupils. Eustace Smith's sign is of little value. More important is an expiratory crow and the cough which resembles whooping cough. Direct percussion over the vertebra gives no information; but D'Espine's sign is very important. The roentgen ray is a great aid in diagnosis, but interpretation of the plates is difficult and a diagnosis of tuberculosis must be made only in conjunction with other findings. A negative Pirquet test, except in infants during the period of incubation, in cachectic conditions, and during the febrile stage of acute infections, means the absence of tuberculous infection. A positive Pirquet reaction indicates a tuberculous infection but not tuberculous disease.

G. MIOCHE [35] has studied the diagnostic value of the Pirquet reaction, the frequency of positive reactions, and the mortality rate of children who react to the test. She affirms that a positive tuberculin reaction always indicates a previous infection with the tubercle bacillus and that there seems little doubt that the bacilli active or latent are still present. Necropsies on individuals who gave a positive reaction always show tuberculous lesions. Except in acute infections, rapidly progressive tuberculous disease, and advanced cachexia, a cutaneous test, negative on repeated examinations, always eliminates a diagnosis of tuberculosis. This has been proved either by the absence of tuberculous lesions at autopsy or by the clinical course of the disease.

O. K. KLERCKER [36] attempted by means of intracutaneous tuberculin tests to differentiate active and inactive tuberculosis. He gave 257 children the intracutaneous test using 0.01, 0.10 and 1.00 mg. tuberculin. The children were divided into three groups: (1) Those with clinical tuberculosis, forty children; (2) those with a suspicious tuberculosis, forty-six children, and (3) those, who after long observations were found free from tuberculosis, 171 children. In the first group, 52.5 per cent. reacted to 0.01 mg. and 30 per cent. to 0.10 mg., a total of 82.5 per cent. Five per cent. of the children gave no reaction even to 1.00 mg. Of these last, one was a case of miliary tuberculosis; the other was a case of peritonitis. Klercker believes that an active tuberculosis, except the very severe forms, will give a reaction to 0.1 mg. and in most instances to .01 mg. of tuberculin. Further clinical study of the cases showed that when a pulmonary tuberculosis is

35. Mioche, G.: The Skin Tuberculin Reaction in Children, Le Nourrisson **8**:42 (Jan.) 1920.

36. Klercker, O. K.: The Local Tuberculin Test in the Diagnosis of Tuberculosis of Childhood, Abstr. Zentralbl. f. d. ges. Kinderh. **19**:523, 1920.

present, a sensitiveness to less than 0.01 mg. tuberculin indicates a weakening of the defense against the infection, and a sensitiveness to less than 0.1 mg. indicates a hopeless outlook.

In the children of the second group a positive reaction to 0.01 mg. tuberculin was regarded as evidence of active tuberculosis, to 1.00 mg. as evidence of latent tuberculosis, and a positive reaction to 0.1 mg., if the children were not in very poor general condition, a healed tuberculosis.

In Group 3, 26 per cent. reacted to the tuberculin, 10 per cent. of these reacting to the smallest dose; and the writer believes that, in spite of no clinical evidences, this also indicates a healed tuberculosis.

From observations on three infants and a careful study of the literature R. DEBRÉ and P. JACQUET [37] have come to the following conclusions regarding the length of time after infection that the tuberculin test becomes positive and the presence or absence of symptoms during this period. After infection with the tubercle bacillus the time when the tuberculin test may be positive varies. The minimum time is six days; the maximum, four months. Variations in this period are due to the age of the patient, the quantity of the infecting material, and whether the cutaneous or intradermal test is used. The period is shorter in new-born than in older children, when the infection is a massive one and when the intradermal test is used. Except in new-born infants, no symptoms occur during this period.

PEYRER [38] reports a case in which the exact time between exposure to tuberculosis and the appearance of a positive intracutaneous reaction was determined. Because of a tuberculosis in the mother and the presence of dullness and bronchial breathing over the left lung in a 7 year old child was thought to have tuberculosis and was placed in a room with another child who had active tuberculosis. He remained there only thirty-six hours. On admission to the hospital the intracutaneous test with 0.001 mg. tuberculin was negative. The test was repeated daily with increasing doses and on the eighth day the child gave a positive reaction with 10 mg.

Peyrer quotes Hamburger, who believes that after infection with 0.5 mg. of bacilli the primary lesion appears in six days; with 0.00001 mg., it appears in twenty-five days. According to Peyrer, a Pirquet test is positive in from six to nine weeks after infection and an intracutaneous test is positive in three weeks. Peyrer says that infection can take place at the distance of one meter and in a very short

37. Debré, R. and Jacquet, P.: The Onset of Tuberculous Infection, Ann. de méd. **7**:122, 1920.

38. Peyrer: Contribution to Tuberculous Infection, Wien. med. Wchnschr. **33**:488 (June 3) 1920.

association; hence, a child should never be in the room with a patient whose sputum contains tubercle bacilli.

W. UNVERRICHT [39] reports a case which shows the greater sensitiveness of the intradermal over the Pirquet test. Two boys, 5 and 6½ years of age, respectively, occupied for twenty-four hours a room with an individual who had open tuberculosis. One boy who sat on the patient's bed gave a positive intracutaneous test with 0.1 mg. old tuberculin forty-five days after exposure. Seventeen days later the Pirquet test became positive. In the other boy who avoided the tuberculosis patient both tests remained negative. Unverricht believes the greater sensitiveness of the intracutaneous test is due to the larger area in which the tuberculin and tissues react and the more rapid absorption of the tuberculin in consequence of the greater pressure with which it is forced into the lymphatics.

As the bovine tubercle bacillus is found more frequently in tuberculosis of children than in that of adults, BERNHEIM-KARRER [40] believes it advisable to use the bovine tuberculin as well as old tuberculin in making the cutaneous test. But it must not be forgotten that because of the close relation between the two forms of tubercle bacilli, patients known to be suffering with tuberculosis of the bovine bacillus type will react to human tuberculin, and that bovine tuberculin produces nonspecific reactions difficult to diagnose from true reactions. In 143 cases of tuberculosis positive results were obtained with human and bovine tuberculin. In eighty-four of these there was no difference between the reactions obtained. In fifty-nine the papule with one tuberculin was decidedly larger than that obtained with the other; or a positive result was obtained with only one form of tuberculin. In eight cases the reaction to old tuberculin was so slight that without the marked reaction obtained with the bovine tuberculin a diagnosis could not have been made. In seven cases there was a reaction only to human and in three cases only to bovine tuberculin. Thus in eleven cases, or 7 per cent., the bovine tuberculin was of greater value than the human tuberculin.

I. SYNWOLDT [41] tested eighty children from 3 to 10 years of age with bovine and human tuberculin. Thirty-nine children had a history of exposure to tuberculosis but no physical findings; thirty-four had a more or less widespread pulmonary involvement; seven had tuberculous peritonitis or scrofula. Seventy-six per cent. of the children in the first

39. Unverricht. W.: Tuberculous Infection, Berl. klin. Wchnschr. **57**:1019, 1920.

40. Bernheim-Karrer: The v. Pirquet Tuberculin Reaction with Bovine and Old Tuberculin, Schweiz. med. Wchnschr. **50**:10 (Jan. 1) 1920.

41. Synwoldt, I.: The Diagnostic and Prognostic Significance of the Cutaneous Reaction with Bovine Tuberculin, Deutsch. med. Wchnschr. **46**:455 (April 22) 1920.

group gave a negative reaction to both tuberculins; 5.2 per cent. gave a positive reaction to both tuberculins, and 17.95 per cent. reacted only to the bovine tuberculin. In the second group, 14.7 per cent. gave a positive reaction to both tuberculins; 29.2 per cent. gave a negative reaction to both tuberculins; 2.9 per cent. gave a positive reaction to the human and a negative reaction to the bovine tuberculin; and 52.94 per cent. gave a negative reaction to the human and a positive reaction to the bovine tuberculin. The third group is too small for any conclusion to be drawn from the results but the high percentage of positive (42.86) reactions with the bovine tuberculin is significant. The author does not believe it possible to differentiate the type of infection by vaccination with both tuberculins but the human organisms seem more sensitive to the bovine tuberculin, so the test is a practical aid in the diagnosis of a tuberculosis, before it can be detected by physical findings. Synwoldt also regards a positive reaction to the bovine tuberculin as a favorable prognostic sign.

E. BJORN HANSEN [42] performed the Pirquet test on the inhabitants of an isolated parish in Norway, in which there had never been a death from tuberculosis. The total population was sixty and fifty-three were examined. The parish has its own school and very rarely do the people come in contact with the outer world. Twenty-one, or 40 per cent., showed a positive, and thirty-two, or 60 per cent., a negative reaction. No one below 16 years of age gave a positive reaction. A road connecting the parish with the outer world is being built and the author thinks it will not be long before the children will show a positive Pirquet reaction.

F. HAMBURGER [43] has noticed that the sensitiveness to tuberculin varies at different seasons of the year. In his experience reactions were decidedly more marked in the Spring. In the Fall children suspicious of being tuberculous rarely gave a positive percutaneous or cutaneous test and the intracutaneous test was only positive with large doses of tuberculin. Children with healed lesions gave a late reaction with 1.0 mg. tuberculin.

Times of increased sensitiveness to tuberculin seem to run parallel to those of increased frequency of tuberculosis. The author offers no explanation of this variation in sensitiveness to tuberculin.

O. LADE [44] has made a study of the microscopic changes in the skin after an intercutaneous tuberculin injection. His method of procedure

42. Hansen, E. Bjorn: v. Pirquet Investigation in a Parish without a Notified Death from Tuberculosis, Tubercle **1**:359 (May) 1920.

43. Hamburger, F.: Variations in Sensitiveness to Tuberculin at Different Times of the Year, München. med. Wchnschr. **67**:398 (April 2) 1920.

44. Lade, O.: The Capillary Microscopic Picture of the Intracutaneous Tuberculin Reaction, Arch. f. Kinderh. **68**:58 (Aug.) 1920.

was as follows: A dilution of 1:1000 or 1:100 of old tuberculin was injected through a very fine needle into the upper layer of the skin. Sufficient tuberculin was used to make a wheal 2 to 3 mm. in diameter. The skin was then made transparent by liquid petrolatum and magnified thirty-five times by means of a Zeiss microscope with a No. 3 objective and a No. 2 eyepiece. Direct sunlight was used for illumination. Directly after injection, when the white wheal is still present, there is seen microscopically a pale area in which the finer skin furrows disappear and the larger ones become narrowed to fine lines. The point of injection appears as a red canal at the end of which is a small amount of blood. A half hour after the injection, when the wheal has entirely disappeared, the skin furrows also have entirely disappeared, but the blood vessels are again plainly visible. After two and a half hours the furrows are again seen and after four hours the skin appears to be normal, except for a slight redness along the site of the injection. Six hours after the injection the redness again becomes intense and the furrows and the outlines of the blood vessels become less and less plain, as this redness increases. Twelve hours after injection well filled blood vessels are seen at the edge of the lesion, where the skin is paler. From eighteen to twenty-four hours after the injection, when a positive reaction can be determined microscopically, all the structures of the skin are blotted out by the diffuse inflammatory redness. The picture then remains stationary for from one to one and a half days, when the redness begins to fade and the blood vessels are again seen at the edges of the lesions. In the center, dark hemorrhagic points appear in the red background. These are the ends of the loops in the papillary bodies of the skin. The vessels of the subcapillary network become more marked than is normal and the skin furrows again become visible. On the third and fourth day the entire process has retrograded and there is a beginning scaling of the horny upper layers of the epithelium. The retrograde process lasts days or weeks, and if the reaction is observed at the end of the third week, besides the scaling there are found present in the horny layers of the epithelium homogeneous transparent masses, which can be lifted out with the point of a needle.

The changes which occur in the first half hour are not specific of tuberculin injections but are produced by injection of physiologic solution of sodium chlorid also; those which occur later, however, are specific, so that by means of this method it can be determined in a few hours whether a reaction is positive or negative.

G. BLECHMANN [45] found that the Pirquet tuberculin test in children aged from 1 to 15 years, when positive, is accompanied by a local glandular reaction in 56 per cent. of the cases; when negative, by a local

45. Blechmann, G.: The Adeno-Cutaneous Reaction to Tuberculin, Rev. de la Tuberc. **1**:45, 1920.

glandular reaction in 16 per cent. The glandular swelling occurs the day after the appearance of the cutaneous reaction and usually persists for two days, though sometimes it lasts longer. When the cutaneous test is repeated, the glandular reaction is not so marked.

C. PESTALOZZA [46] tested seventy-two children for the regional cutaneous reaction. He substantiates the findings of Pisanis and other writers that reactions over the tuberculous lesions are stronger than controls made elsewhere. The explanation is that over the tuberculous lesions the lymphatics are more developed. This is, however, not a regular finding and has no significance.

H. ELIASBERG and E. SCHIFF [47] made a study, based on the researches of Wildbolz, who found in the urine of patients with active tuberculosis a specific antigen, which caused a tuberculin reaction at the site of vaccination. In preparing the urine, the authors followed the technic of Wilbolz. It was obtained in a sterile manner and evaporated to one-tenth its volume in a vacuum. The temperature of the water bath could be raised to only 70 because of the danger of destroying the tuberculin-like substance. After a cooling process the urine was filtered through a filter saturated with a 2 per cent. solution of phenol. Directly after the injection there appeared a large wheal with a large surrounding area of hyperemia. This traumatic reaction disappeared in from one to two hours. The character of the reaction was decided in forty-eight hours. A positive reaction consisted of redness and infiltration, which depended on the substance resembling tuberculin in the urine. A central superficial necrosis occurred in severe reactions.

Wildbolz emphasized that a reaction is to be expected only in cases of active tuberculosis and every patient tested with urine must have a control tuberculin test.

Eliasberg and Schiff's material consisted of forty cases of various forms of tuberculosis in children. They conclude from the study that the urine reaction is specific but gives no proof as to the activity of the lesion. The results in three patients with pleuritis serosa were especially interesting. In two there was no tuberculin-like substance in the urine and in one only a very slight amount—results which make it appears questionable whether every case of pleurisy in children is of tuberculous origin.

The authors do not put so much value on the procedure as did Wildbolz, but they believe the method worth further consideration.

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46. Pestalozza, C.: The Reginal Cutaneous Reaction in Infants, Pediatria. **28**:171 (Feb. 15) 1920.

47. Eliasberg, H. and Schiff, E.: The Wildbolz Auto-urine Reaction in Tuberculous Children, Monatschr. f. Kinderh. **19**:5 (Oct.) 1920.

R. OFFENBACHER [48] does not believe the Wildbolz test to be reliable, for he obtained only three positive reactions in twenty cases of active tuberculosis. In a number of instances the Mantoux test (1:10000) was positive and the Wildbolz negative, according to the writer, therefore its presence shows only a possibility of an active tuberculosis.

F. ARLOING, PIERY, LEDRU and CORDIER [49] were unable to verify Wildbolz's assertion that the uro-intradermal test allows of differentiation between active and inactive lesions. They believe the test to be of equal value with the intradermal tuberculin test.

O. IMHOF [50] reports his results with the autourine and autoserum tests for the activity of tuberculosis in eighty cases. The results of both tests, with few exceptions, coincided; but the reaction was somewhat weaker with the autourine test. Both reactions were positive in the presence of an active tuberculosis, provided the skin was sensitive to tuberculin. Both reactions were negative in nontuberculous patients. The autoserum reaction is of more value when a disturbed kidney function interferes with the excretion of antibodies.

BECKER [51] uses the roentgen ray to follow the course of tuberculosis. He says repeated roentgenograms often give a surprising and characteristic picture. They sometimes show that diffuse pulmonary shadows are due not to the tuberculous process but to an inflammatory exudate in the neighborhood of one or more tuberculous areas. This is evident from the disappearance of these shadows after a number of years. Becker is of the opinion that roentgen-ray examination shows changes in the lung when clinical manifestations are entirely lacking; and that is proves also that active tuberculosis in children, if they receive proper care, can recede and leave only scar tissue.

From the study in 190 roentgenograms R. SPERLING [52] draws the following conclusions as to the localization of the tuberculous lesions in children. The primary lesion is usually in the upper lobe and lymphatic involvement of the primary stage manifests itself by changes in the hilus glands. Apical lesions are rare. In the second stage acute generalization is frequent. In older children there is a tendency to chronic indurated forms, which more often affect the right lung.

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48. Offenbacher, R.: A Study of the Wildbolz Method of Determining an Active Tuberculous Lesion, Ztschr. f. Tuberk. **32**:355 (Sept.) 1920.

49. Arloing, F., Piery, Ledru and Cordier: The Wildbolz Autourine Reaction, Abstr. Rev. de la Tuberc. **1**:183, 1920.

50. Imhof, O.: The Wildbolz Autourine Reaction as a Proof of Active Tuberculosis, Schweiz. med. Wchnschr. **50**:1033 (Nov. 11) 1920.

51. Becker: The Course of Tuberculosis in Childhood as Seen in Roentgen-Ray Plates, Beitr. z. Klin. d. Tuberk. **45**:391 (Nov. 25) 1920.

52. Sperling, R.: The Localization of the Lesion in Pulmonary Tuberculosis by Means of the Roentgen Ray, Abstr. Zentralbl. f. d. ges Kinderh. **10**:64 (Dec. 14) 1920.

Isolated lesions in the left side and in both lungs increase with the age of the child. In older children the upper portions of the lungs, especially the infraclavicular regions, are often affected. The process spreads to the apex in one half of the cases. Also in older children bilateral lesions frequently occur at the base of the lung.

In the third stage cavities occur. These are usually single and unilateral and formed in the upper lobe.

D. GRINGOLD [53] describes a symptom which in the last seven years has been of considerable service to him in making a diagnosis of tuberculous basilar meningitis and which he calls a "reflex" strabismus. It is elicited by flexing the head on the chest, when there develops either a bilateral or a unilateral internal strabismus which lasts as long as the head is kept in a flexed position and disappears as soon as the head is relaxed. In some cases the strabismus is accompanied by a retraction of the upper eyelids and by a contraction of the pupils. The author believes a reasonable explanation of this early "reflex" strabismus is that when the head is flexed the already increased pressure at the base is suddenly augmented and causes pressure on the abducens nerve with a paresis of the external rectus, or on the oculomotor nerve, with a spasm of the internal rectus.

In twenty-three cases of tuberculous meningitis, G. GENOESE [54] examined the spinal fluid and urine for acetone. In twenty cases there was an increased amount of acetone in the urine and acetone was found in the spinal fluid. In three cases in which there was but little acetone in the urine none was found in the spinal fluid.

PROGNOSIS

J. W. LANGENDÖRFER [55] followed the fate of 269 children in fifty families of whom one parent or both were treated for tuberculosis at the Bonn Clinic. He found that 146, or 54.2 per cent., suffered from the disease of the parents. Of 119 children in nineteen families of which the father had tuberculosis, the mortality from tuberculosis was twenty-one, or 17.6 per cent. Of 150 children in thirty-one families of which the mother had tuberculosis, the mortality from tuberculosis was thirty-nine, or 26 per cent. So, when the mother was affected, the mortality was higher than when the father was affected. Langendörfer found also that the morbidity and mortality from tuberculosis were greater in large than in small families and the youngest children in

53. Gringold, D.: An Early Diagnostic Sign of Basilar Meningitis, Arch. Pediat. **37**:19 (Jan.) 1920.

54. Genoese, G.: Acetone in the Spinal Fluid in Tuberculous Meningitis, Pediatria. **28**:449 (May 15) 1920.

55. Langendörfer, J. W.: The Fate During the War of Children of Tuberculous Parents, Ztschr. f. Tuberk. u. Heilstättenw. **33**:150 (June) 1920.

the family were the ones most frequently infected. The morbidity and mortality were greatest during the first five years of life and just before or after puberty.

M. M. RIBADEAU-DUMAS and H. BÈCLERÈ [56] report a case which shows that tuberculosis in infants does not always end fatally. The patient was a 13 month old baby who at 9 months had been cared for by a servant with open tuberculosis. The child developed slight temperature elevation and failed to gain in weight. There were absolute dulness and feeble respiration over the entire right lung. In the course of a month this became limited to the right scapulovertebral space, in which there also was bronchial breathing. Emaciation and whooping cough-like attacks and diarrhea developed. The Pirquet test was positive. Six years later the child again came under observation. He was well and strong and had no abnormal findings in the chest.

EICHELBERG [57] also reports two cases which show that the prognosis of pulmonary tuberculosis in young children is not so unfavorable as is usually supposed.

The first patient was taken to him when 13 months old and at that time was extremely ill. He was coughing day and night and was dyspneic and very hoarse. There was a tuberculous lesion on the right parietal bone. The cutaneous tuberculin test was positive and, in spite of practically negative physical findings, the roentgen ray showed a somewhat dense shadow over the entire right side. Under treatment the child gradually improved and a second roentgenogram, taken six months later, showed the shadow was less dense. At the time of writing the child was 21 months old and in very good condition. The voice was still hoarse and there was slightly impaired resonance over the right side. The lesion of the parietal bone was healing.

The second patient was seen at 2 years and 9 months of age. When 2 years old she was taken ill with cough, fever, loss of appetite and sweating. At first there were no definite pulmonary findings. Later the percussion note on the right side showed impaired resonance. The fluoroscope showed a definite shadow at the right apex and one extending downward from the upper part of the hilus into the right upper lobe. The Pirquet test was positive. The child was treated with heliotherapy and four months later appeared perfectly well. The roentgen-ray findings were unchanged.

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56. Ribadeau-Dumas, M. M. and Bèclerè, H.: The Evolution of the Initial Lesion of Pulmonary Tuberculosis in an Infant, Abstr. Arch. de méd. d. ènf. **23**:728 (Dec.) 1920.

57. Eichelberg: Prognosis of Tuberculosis in Childhood, Monatschr. f. Kinderh. **18**:123 (May) 1920.

The belief that tuberculosis in infants is always fatal has undergone a change. External tuberculous lesions in young children have been known to heal and at necropsies reparative processes have been observed in tuberculous lesions of the lungs in even very young infants. Furthermore, many times recovery from pulmonary tuberculosis in infants has been reported in the literature.

L. BENARD and R. DEBRÉ [58] have made a study of the infants of tuberculous mothers sent to the Laennec Tuberculosis Hospital with regard to the frequency of infection and the mortality of infected infants. Of fifty-eight infants, forty were found to be tuberculous. In the case of the eighteen who were free from tuberculosis, separation from the mothers took place after from eight hours to six months of contact. Of sixty-five infants of nontuberculous mothers sent to the hospital by mistake, only eight became infected, three in the hospital, two in another hospital, and three through the father.

Of the forty infants infected only twelve died. The length of contact with the mother in these cases was from two to three months; in one case thirteen days. In all of these cases death occurred in the month that followed separation.

The authors draw the following conclusions: After four months of contact with a tuberculous mother an infant is presumably infected. All infants infected by contact with their mothers do not die; if the infant is still alive one month after separation he will probably survive. This is contrary to the opinion that tuberculosis of the first year of life is incurable.

STATISTICS AND PROPHYLAXIS

J. BARTSCHMID [59] made an analysis of the histories of patients admitted to the University Children's Hospital of Munich from 1912 to 1919, in order to ascertain the effect of war conditions on the frequency of tuberculosis among the children of that city.

Six hundred and seventy-five patients were admitted in the prewar years 1912 to 1914, and 1,004 during the years 1915 to 1919. Thirty-six per cent. of the children admitted during the prewar years and 47.6 per cent. of those admitted during the years of the war gave positive tuberculin reactions. The increase did not affect infants or children between 7 and 8 years, but all others, and especially children between 3 and 4 years. The children of Munich, then, were infected earlier in war times than in prewar times. The statistics showed also

58. Benard, L. and Debré, R.: The Mode of Infection and of Prevention of Tuberculosis in Young Infants, Bull. de l'Acad. de méd. Par. **84**:86 (Oct. 5) 1920.

59. Bartschmid, J.: The Result of War Conditions on the Frequency of Tuberculosis in the Children of Munich, München. med. Wchnschr. **67**:957 (Aug. 13) 1920.

that the mortality from tuberculosis in children was increased only in 1916 and chiefly affected children from 1 to 5 years of age. This was due probably to the fact that during the first two years all able bodied men were in military service, the women at work, and the children left in care of sick and incompetent individuals.

A comparison of these statistics with those of other cities shows that during the war years there was less tuberculosis in the children of Munich than among the children of other German cities, but there was an earlier infection and an increase in the severe forms.

H. DAVIDSOHN [60] performed the Pirquet test on a large number of orphan children in an ambulatory clinic of Berlin to obtain an idea of the increase in frequency of tuberculosis during the war. During 1919, from 5.4 to 6.1 per cent. were found tuberculous, a marked increase over the figures of 1913. Moreover, infection took place at an earlier age; while in 1913, 30 per cent. gave a positive tuberculin test at 4½ years; in 1919, 30 per cent. of the children gave a positive reaction at 2½ years. There seemed to be a decrease in the number of positive reactions in the children of 5 and 6, but this was due simply to the absence of antibodies because of emaciation from improper food and not to the absence of tuberculous infection. Davidsohn found also that, when the intracutaneous test was used, a much greater number of positive reactions were obtained. His tests, then, showed, that among the 2 year old orphans every second child was infected and among the 6 year old children two of every three were infected.

E. ROMINGER [61] found that in 1919 fewer children gave a positive Pirquet reaction than in previous years. Routine tests in 1917 gave 41 per cent. positive reactions; in 1918, 39 per cent., and in 1919, 31 per cent. And this occurred in spite of the material increase in tuberculosis among children since the war. Rominger believes an explanation is found in the fact that from general malnutrition there are changes in the skin which inhibit the reaction and he concludes that a negative Pirquet test is of little value and must always be followed by an intracutaneous test.

P. KESSLER [62] has compared statistics of the number of positive Pirquet reactions in children compiled before the war with those which he has collected in the Rostock clinic since the war. He finds that among children from 1 to 2 years of age there were from three to four times as many positive reactions; among children from 2 to 7

60. Davidsohn, H.: The Increase of Tuberculosis in the Children of Berlin, Ztschr. f. Kinderh. **26**:178 (Aug.) 1920.

61. Rominger, E.: Experience with Tuberculin in the Diagnosis of Tuberculosis in Childhood, Monatschr. f. Kinderh. **18**:424 (Aug.) 1920.

62. Kessler, P.: Increase in Frequency of v. Pirquet Reactions During the War, Beitr. z. Klin. d. Tuberk. **44**:1 (April) 1920.

years there were twice as many, and between 7 and 10 years, one-third again as many as among children of the same age before the war.

F. GARLAND COLLINS [63] defines the pretuberculous child as follows: A child whose vitality remains materially lowered and in whom some or all of the following conditions persist: frequent rise of temperature, enlarged lymphatic glands, loss of weight or failure to gain in weight, chronic bronchial catarrh, loss of appetite, carious teeth with stomatitis, or a general strumous condition. Especially is this true if these symptoms are associated with a family history of tuberculosis or contact with a tuberculous person. Not all these children develop tuberculosis. A certain percentage have a high degree of resistance and respond readily to ordinary treatment, but the majority become definitely tuberculous.

Chief among the various forms of treatment are (a) open air schools, residential or daily; (b) convalescent homes; (c) boarding out in the country; (d) tuberculosis dispensaries. Of most value are the residential open air schools.

W. R. P. EMERSON [64] was able to bring 189 tuberculous children up to an average of nearly double the expected weight in a nutrition class, conducted in connection with the outpatient department of the Boston Consumptive Hospital. Emerson believes that the problem of tuberculosis is for the most part a problem of nutrition. He says that if children are made well in a sanatorium, they get health; but, if they can be made well in their own homes, they get health, health education, and character. Nutrition work, which covers a new and hitherto neglected field in medicine, must be carried on with proper authority. It cannot fit in as an adjunct to other programs; but other programs must be adjusted to fit the problem of nutrition, which is the fundamental problem of tuberculosis. With the proper cooperation of the four factors that safeguard the child's health, namely the home, medical care, the child's own interest, and the school, all children can safely be brought to normal health.

A. LEVINSON [65] discusses the questions what to do with children whose parents are tuberculous but who themselves have not contracted the disease and what to do with children who have already contracted the disease.

In regard to the first, children must not come in contact with open cases of tuberculosis. The tuberculous member of the family or the

63. Collins, F. Garland: The Pretuberculous Child, Tubercle **1**:454 (July) 1920.

64. Emerson, W. R. P.: Nutrition Classe and Tuberculosis, Boston M. & S. J. **183**:361 (Sept. 16) 1920.

65. Levinson, A.: Sociological Phrases of Tuberculosis in Children, Mod. Med. **2**:539 (Aug.) 1920.

child must be removed. When the parent, or other member of the family, is a closed case, the fate of the child depends on whether the father or the mother is the offending party. If the father is tuberculous, he should be removed to a sanitarium, for no one can predict when he will become an open case; and the child should remain with the mother. If the mother is a closed case, the child should preferably be removed from the house. When possible, these children should be sent to a special home, where they can be under the supervision of a physician and nurses and where they can receive special attention.

In regard to the treatment of infected children, Levinson discusses only that of latent tuberculosis; and this depends entirely on home conditions. If home conditions are good, i. e., if the child can get plenty of sunshine, good nourishing food and enough sleeping space, and if there is no open case in the family, the child can be treated at home. A child with latent tuberculosis may be sent to school; if possible, to an open air school. Rest is one of the principle requirements of a tuberculous child.

If home conditions are not good, the child should be sent to a sanitarium. The author thinks that the founding of special sanitariums should arouse a great deal of interest among physicians and social workers.

M. KLOTZ [66] regards pulmonary tuberculosis of infants as being infectious, even when no tubercle bacilli are found in the sputum, and emphasizes that these children should not be allowed to remain in a ward with others. He reports the case of a child in a hospital ward who had coughed for two months, gave a positive Pirquet reaction, and had finally died of tuberculous meningitis. In the course of the following few months three caretakers and five children of the ward developed tuberculosis.

W. J. DOBBIE [67] agrees with all writers as to the great danger to the infant of contact infection. In children over three years of age, he emphasizes the importance of avoiding massive but not a casual infection. As immunity is essential for the welfare of the child, Dobbie believes the period between infancy and adolescence the most opportune time to invite infection for the purpose of immunization.

A. and T. STRÜBELL [68] have made an exhaustive review of the literature on the passage of immune bodies from the milk and of intestinal absorption of immune bodies; and they report their own

66. Klotz, M.: The Danger of Infection from Tuberculosis in Infants, München. med. Wchnsch. **67**:964 (Aug. 13) 1920.

67. Dobbie, W. J.: The Prevention of Tuberculosis, Am. Rev. Tuberc. **4**:23 (March) 1920.

68. Strübell, A., and Strübell, T.: Immune Milk and Prophylaxis of Tuberculosis, Beitr. z. Klin. d. Tuberk. **45**:38 (Nov. 25) 1920.

observations on the passage of antibodies and antigens from placental circulation and from the milk into the fetus.

They believe it certain that in women antibodies, antigens, and partial antigens pass into the fetus through the fetal circulation; and in all probability in cows. Moreover, it has been proven that antibodies and antigens, in large amounts, both in women and cows, pass into the milk. The mammary glands play not merely a passive rôle in allowing this passage of the antibodies but produce and elaborate them. Absorption of these antigens from the milk into the blood serum of calves during the first months after birth has been proved. That this is not only a passive immutivity but an active immunity of long duration is evident through the presence of a positive intracutaneous reaction. The inability to produce a positive intracutaneous test in the infant seems to be due rather to the method of experimenting than to the inability of the child to react to the tuberculin. It remains to be shown just how long this immunity lasts and from how severe an infection it protects. When this is ascertained, the authors think, a way will be found to use the milk of immune women and cows for infants and calves and a great step forward will be made in the prophylaxis of tuberculosis.

TREATMENT

M. SOLIS-COHEN [69] discusses a method to determine the appropriate dose of tuberculin for the individual child. He first makes the following test for tuberculin hypersensitiveness. Simultaneously, he injects intracutaneously, in the forearm one ten millionth mg., one millionth mg. and one hundred-thousandth mg. If no reaction occurs in from twenty-four to forty-eight hours, one ten-thousandth, one thousandth and one hundredth of a mg. are injected similarly in the other arm. If still no reaction occurs, one tenth of a mg. and 1 mg. are then injected, and, if necessary, at a still later time 10 mg.

The smallest dose that produces a distinct local reaction the author administers therapeutically either by mouth or subcutaneously. If this dose causes increase of appetite, reduction of temperature, a general feeling of improvement, it is repeated every three or five days until it loses its effect, when it is gradually increased until a favorable reaction is again produced. If no general reaction is produced by the smallest dose which causes a local reaction it is repeated for several weeks and is then increased. Should any dose produce an unfavorable reaction, such as rise of temperature, anorexia, malaise, it is reduced. At intervals tests for hypersensitiveness are again made by injecting intracutaneously into the forearm the dose the patient is taking and doses one-tenth of and ten times this amount.

69. Solis-Cohen, M.: A Method for Determining the Appropriate Dose of Tuberculin for the Tuberculous Child, Arch. Pediat. **37**:641 (Nov.) 1920.

If no reaction occurs from any of these, one hundred times, one thousand times and ten thousand times the amount the patient is taking is injected intracutaneously. If the amount producing the intracutaneous reaction is greater than the amount which is being given therapeutically the latter dose is increased rapidly until it corresponds with the former.

The author uses tuberculin Rückstand (T.R.) for the injections. He reports the value of this method in nineteen cases in children whose initial doses varied from one hundred-millionth to one hundredth mg. and were increased from ten to 120,000 times over a period of from one to twenty-one months, practically without producing an unfavorable reaction in any case. A large proportion of the children showed improvement in general condition, reduction in temperature and gain in weight.

R. C. Holt [70] believes that infants are infected in early postnatal life, usually from their mothers, and that this is the time to use tuberculin injections as a curative agent. He points out that the systematic use of tuberculin in infancy has two objects: first, as a test to show how many babies are infected; and second, to be the first installment of treatment in those already infected. Whenever a child gives a positive reaction, further graduated injections should follow, until a reaction fails; and the weight should be used as an index of the effects of the tuberculin. In this way, then, one could secure reasonable assurance that every child a year old is free from tuberculosis. Probably a second test would be necessary for those still exposed to infection. Holt suggests injecting one-fifth of one millionth of 1 c.c. for an infant aged 3 months. Most tuberculous babies show a rise in temperature of 2 degrees during the first six hours after the injection.

J. Gracia del Diesto and B. Cordeo [71] advocate the intradermal tuberculin treatment of tuberculosis in children. They have used it for three years and find it free from dangers and difficulties of the subcutaneous method. Their technic is as follows: A needle from 1½ to 2 cm. long, with a short, sharp end, which easily stays in the skin, is used. Six solutions are made. The first contains one part of tuberculin and nine parts of a solution of ½ per cent. sodium chlorid and ½ per cent. phenol; the second contains one part of this solution and nine parts of the phenol-sodium chlorid solution; the third contains one part of solution No. 2 and nine parts of the phenol-

70. Holt, R. C.: A Plea for the Tuberculinization of Babies, Tubercle **2**:54 (Nov.) 1920.

71. Gracia del Diesto, J. and Cordeo, B.: Intradermal Tuberculin Treatment of Pulmonary Tuberculosis in Children, Arch. Espan. d. Pediat. **4**:20 (Jan.-Feb.) 1920.

sodium chlorid solution, etc. Only 1/10 cm. of the solution judged best for the case is used for the first injection. In cases of tracheobronchial adenopathy, as the sensitiveness to tuberculin is slighter than in pulmonary forms, the more concentrated solutions can be used in the beginning of the treatment. According to Jeanneret, the diameter of the macule which results from the injection should not be more than from 10 to 15 mm. If it is, a weaker solution must be used; but the authors generally obtained a macule of from 20 to 30 mm. Injections are given once a week. If symptoms of anaphylaxis, as increased in size of papule with each injection, temperature, and loss of weight, arise the treatment is stopped. Weight is a valuable criterion of the benefit or harm of the tuberculin treatment. The authors are well satisfied with the results obtained by this method.

H. MUCH [72] has lately published a monograph (translated by M. Rothschild) on the diagnosis and the treatment of tuberculosis in children. In it he goes into detail with regard to the so-called partial antigen treatment of Deycke-Much, and he says there can be no cure without immunity, while progress in treatment depends on the maintenance of immunity. His partial antigens, by which immunity is maintained, are obtained by so treating cultures of tubercle bacillus that the acid-fastness of the bacilli disappears and there is obtained a substance which is referred to as M. Tb. By filtering M. Tb. a water soluble substance, containing the toxin of the tubercle bacillus, is obtained. This represents the pure tuberculin and is designated as L. The water-insoluble residuum is called M. Tb. R. and by treating this with alcohol and ether the three partial antigens are obtained. The portion soluble in alcohol contains the fat acid lipoids and is called by the author F.; the portion soluble in ether contains the neutral fats and is called N., the insoluble portion belongs to the group of nucleo-proteins and is designated as A. Only the M. Tb. R. and the special antigens A. F. N. are used in the treatment of tuberculosis.

Before treatment is started, intracutaneous injections are made with the partial antigens, in order to determine to which the patient is already immune and the degree of immunity. The degree of immunity is shown by the size of the papule and surrounding inflammatory area which results from the injection. If a positive reaction is obtained with N. partigen and a negative reaction with A. partigen, the patient is treated chiefly with A. partigen. Very small doses only are used for treatment. The author believes this method to be of special value in the treatment of bronchial gland tuberculosis.

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72. Much, H.: Tuberculosis in Children; Its Diagnosis and Treatment, Translation by M. Rothschild, MacMillan Comp., 1921.

R. PIPEL [73] reports his experience with the partigen treatment of tuberculosis in children. His observations were made on thirty-two children from 3 to 12 years of age. Twenty-six had pulmonary tuberculosis, four had bronchial gland tuberculosis, one had osseous tuberculosis, and one had peritoneal tuberculosis. Five of the children with pulmonary tuberculosis were dismissed as cured and fourteen with the condition improved. In three the condition remained stationary, in two it became worse. Five children died.

In the four children with bronchial gland tuberculosis the general condition improved but the roentgen-ray findings remained unchanged. The child with osseous tuberculosis improved and the one with tuberculosis peritonitis died. Pipel's therapeutic results, on the whole, were favorable, but no more so than results observed in another group of patients under observation at the same time.

A. CZERNY and H. ELIASBERG [74] have treated the cachexia of tuberculous children with a foreign proteid (horse serum) in the hope of increasing their resistance. At first 10 c.c. was injected twice a week but as severe anaphylactic manifestations were obtained from 1 to 2 c.c. daily were given instead. Thirty very sick practically moribund children, suffering from pulmonary and abdominal tuberculosis, were treated in this way. In twelve good results were obtained. The children looked better, gained in weight, and no longer had fever. These results were obtained only after weeks of treatment. The treatment with horse serum influenced also the manner in which the children reacted to the tuberculin test. Children who gave a "cachectic" reaction before treatment later gave a normal tuberculin reaction. Focal reactions were never observed in the tuberculous lesions.

H. ELIASBERG [75] recommends establishing a pneumothorax in pulmonary tuberculosis in infants and children. At first he used the procedure in children with advanced lesions only but later also in those with early lesions; at first, too, only in those with unilateral, but later in those with bilateral lesions. In instances of bilateral lesions the lung more severely affected was treated first, then the other. The author obtained favorable results in cases of hilus tuberculosis and pulmonary tuberculosis with cavity formation. Until the attempt is made, it is impossible to tell whether a pneumothorax can be produced or whether the pleural cavity is obliterated by adhesions. At first nitrogen was used, later atmospheric air. To be of any value, the

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73. Pipel, R.: Review of Experience since 1917 with Partigen Treatment of Tuberculosis in Children, Wien. klin. Wchnschr. **33**:402 (May 6) 1920.

74. Czerny, A. and Eliasberg, H.: The Treatment of Tuberculous Cachexia with Foreign Proteid, Monatschr. f. Kinderh. **19**:107 (Oct.) 1920.

75. Eliasberg, H.: The Treatment of Tuberculosis in Children with Pneumothorax, Monatschr. f. Kinderh. **19**:105 (Oct.) 1920.

pneumothorax must be maintained, until the lungs are healed—for a period, that is, of at least two or three years.

W. BAENSCH [76] has used tebelon with nineteen patients, mostly children, suffering from bone, joint, gland and skin tuberculosis. Tebelon is a preparation consisting of the isobutyl esters of fatty acids of tubercle baccillus. Stoeltzner, who first isolated the substance, believed it stimulated the production of antibodies. Baensch injected 1 c.c. into the back every third day. No ill effects attended its use. From his experience the author thinks that tebelon is not a specific for tuberculosis but that it shortens the duration of surgical tuberculosis in children.

A. REUTER [77] reports his results with tebelon, which extended over a period of seven months. He used 1.1 c.c. twice a week. The greatest number of injections was thirty-eight. From this experience Reuter believes tebelon is an indifferent agent and has no effect on the human organism.

The experience of F. LEHNERDT and M. WEINBERG [78] with tebelon extended over a period of three years. In all there were treated ninety patients of whom ten were adults with acute phthisis; eight had lupus; thirty-three were children with severe clinical tuberculosis; thirty-seven were children with scrofula. The conclusions drawn from the study were that tebelon has no influence on tuberculosis in adults; it has a favorable effect on lupus but this is not permanent. It has no effect on pulmonary tuberculosis of childhood, when at an advanced stage. Its use is only advised when the process is well localized and the children are in good physical condition. In scrotula, however, it seems to be a very useful remedy, a favorable influence was observed in all the cases. At first there was a softening of the infiltrations of the skin or glands—then the secretion gradually stopped—all inflammatory areas showed a tendency to granulate and healing took place more quickly than was expected. Scrofulous eczemas and phlyctenular conjunctivitis were soon cured. Swelling of the glands disappeared and the general condition of the patient improved.

A. DU FOURT [79] advises heliotherapy in the treatment of mediastinal adenopathy in children. The treatment is begun by exposure of the lower extremities. After the eighth day the chest is exposed for five minutes daily and, if the treatment is tolerated, the exposure is increased

76. Baensch, W.: Tebelon in the Treatment of Surgical Tuberculosis, München. med. Wchnschr. **67**:1009 (Aug. 27) 1920.

77. Reuter, A.: Treatment of Tuberculosis in Children with Tebelon, Monatschr. f. Kinderh. **19**:34 (Oct.) 1920.

78. Lehnerdt, F. and Weinberg, M.: Tebelon in the Treatment of Human Tuberculosis, Ztschr. f. Kinderh. **26**:215 (Sept. 13) 1920.

79. Du Fourt, A.: The Treatment of Mediastinal Adenopathy with Heliotherapy, Arch. de méd. d. énf. **23**:436 (July) 1920.

to two hours daily. Pulse and temperature must be watched closely. If there is pulmonary as well as gland involvement, the child should be put to bed for a week before the treatments are begun; and thoracic exposure should never exceed ten minutes.

In mediastinal gland tuberculosis physical signs and roentgen-ray shadows usually disappear in four or five months, but, if there is pulmonary disease, the duration is much longer. In some patients heliotherapy seems to aggravate the glandular condition and is contraindicated. Young infants do not stand the treatment well. Erythema and a rise of temperature to 39 or 40 C. are warnings against too long exposures.

I. S. TROSTLER [80] recommends the roentgen-ray treatment in tuberculous adenitis. When no breaking down or liquefaction has taken place, brilliant results are the rule in 80 per cent. of the cases. Even when the glands have broken down and are draining, the roentgen ray will often produce reduction in size and softening of the scar tissue. If the glands have broken down and are not draining, it is better to aspirate the contents, before treatment is commenced. Aspiration can be repeated as often as fluid appears. A very useful and efficient adjunct to roentgen-ray treatment in cases in which suppuration has continued for a long time is the swabbing out of the sinus with a mixture of equal parts of phenol and tincture of iodin.

C. E. FIELD [81] does not advocate radium to take the place of surgery in the treatment of tuberculous adenitis but believes it to be of great value in the treatment of this condition. In thirty-two patients treated during four years the process was arrested and apparently cured in twenty-seven; three patients were lost sight of, and one died from pulmonary tuberculosis two years after treatment.

H. GAUVAIN [82] describes the Teloar Crippled Hospital for tuberculous children. The place was chosen because of abundant sunshine, extensive shore line with considerable tidal excursion, sandy soil, slight or moderate rainfall, lack of trees, clear atmosphere free from dust, hills protecting from the cold and winds, bracing climate, beach adequate for unrestricted use of the patients. The hospital itself has an extensive veranda so constructed that the patients need not leave it, even during rain, and especially designed awnings pull down over the beds; the mattresses are heated by electricity, which is the best and most labor-saving method of keeping the patient comfortably warm.

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80. Trostler, I. S.: The Treatment of Tuberculous Adenitis with Roentgen Ray, Am. J. Clin. Med. **27**:804 (Dec.) 1920.

81. Field, C. E.: The Treatment of Tuberculous Adenitis with Radium, Long Island M. J. **14**:424, 1920.

82. Gauvain, H.: The Care of Tuberculous Children, Brit. J. Tuberc. **14**:49 (April) 1920.

A valuable feature of the institution is the postgraduate course in surgical tuberculosis.

T. H. MARTIN [83] describes the hospital school for the treatment of surgical tuberculosis in children at Seasowe-Cheshire. It is built within 300 yards of the sea, fully exposed to winds which sweep from the Irish Sea. It is constructed on the block parallel system. Each block consists of two stories with twenty-four to thirty beds on each floor. The wards face due north and are light and airy. On the southern aspect are large sun balconies on which beds are always kept, except in the severest weather. Abundance of fresh air, sunshine and good food are the principal factors in treatment. Great importance is placed on heliotheraphy. Carefully planned school-work with hospital treatment has proved a great success.

A. W. HOLLIS and I. H. PARDEE [84] have collected from the literature reports of thirty-eight cases of tuberculous meningitis with recovery of the patient and report two cases of their own. They report two other cases in which a probable diagnosis of tuberculous meningitis was made. Their method of treatment was to use intraspinal injections of antimeningococcic serum with frequent spinal drainage. They consider that intraspinal injections of antimeningococcic serum have two distinct actions. First it adds to the spinal fluid certain antibodies, which it is unable to develop itself and second it introduces within the dura a foreign proteid in the form of horse serum.

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83. Martin, T. H.: The Hospital School for Treatment of Surgical Tuberculosis in Children, Brit. J. Tuberc. **14**:145 (Oct.) 1920.

84. Hollis, A. W. and Pardee, I. H.: Recovery from Tuberculous Meningitis after Treatment with Intraspinal Injections of Antimeningococcic Serum, Arch. Int. Med. **26**:49 (July) 1920.